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NEUROLOGY IN THE GENERAL HOSPITAL*

BY

HENRY MILLER, M.D., F.R.C.P.

Physician in Neurology, the Royal Victoria Infirmary, Newcastle upon Tyne

To discuss the differences between the practice of neurology in the general and the special hospital is to take advantage of the traditional licence of the opening lecturer to deal with the general rather than with the particular. The subject is one which invites controversy.

Functions of the Special Hospital

The metropolitan special hospital, of which the National Hospital is an outstanding example, fulfils two main functions. An administrative unit of the National Health Service, it provides a court of appeal at a national level in the difficult clinical problem. Such a splendid diagnostic service is difficult to maintain and easy to undervalue, but it is an inestimable boon to every neurologist working outside London, and to his patients. Even apart from other considerations it fully justifies the existence—and the expense—of the special hospital. Together with responsibility for disseminating the highest standard of current clinical practice by teaching and example, it represents, however, only the topical function of the teaching hospital, its more long-term aim being the development and application of new knowledge and new methods.

Of the many physicians trained in neurology at Queen Square most will spend the rest of their professional lives in less specialized institutions. The unequalled standards of systematic case-taking characteristic of the special hospital are equally applicable to the different categories of diagnostic problems encountered there. Laboratory and instrumental methods of the highest calibre may be employed to amplify clinical evidence of the patient's *status*, but the fact is never lost sight of that only a skilfully elicited and interpreted history can lay bare the chain of interlinked events which constitute the "disease" and reveal the nature of the pathological *process* involved. The remarkable precision of the traditional methods of clinical neurology is very much taken for granted here, but it strikes anew the physician who leaves the special for the general hospital: less often than most other branches of medicine is neurology found to degenerate into the shuffling of sheaves of laboratory or radiological reports. Despite the current contributions of the electrophysiologist, it is still the most clinical of specialties, and the trained human mind remains a more ingenious and subtle electronic device for its prosecution than even the electrocorticogram.

The environment of the special hospital undoubtedly favours the cultivation of the highest degree of diagnostic virtuosity, as well as of the most highly developed ancillary skills. It affords unparalleled facilities also for the collection and analysis of groups of rare cases, work superficially unpromising which may, however, at any time throw unexpected light on commoner and more intrinsically important clinical problems. Nevertheless for clinical research in neurology as a whole the general hospital offers opportunities which are in no way inferior, and which are indeed complementary to the more evident ones of the specialized institution.

The differences between the clinical material of the neurologist in the general and in the special hospital are of intrinsic interest, and they raise issues also of importance to any consideration of the future of the subject.

Problems of the General Hospital Neurologist

Every general hospital—even a teaching centre—is primarily a district hospital. The special position of the teaching hospital arises from the fact that it attempts, with more or less success, the difficult task of combining its function as a district hospital—a role as essential from the teaching as from the service point of view—with that of a special reference hospital for the vast but still fairly well defined conurbation around it. Patients come to the neurologist in the general hospital, in the main, first-hand and unselected. Since practically all the important neurological cases in his area will pass through his clinic, he is in a position to assess the incidence and distribution of neurological disorders in the population at large—ecological information which is a source of vital evidence in aetiological studies.

Under such circumstances, for example, the early recognition of small epidemics of nervous disease such as vertigo or infective polyneuritis is easy. More significantly, such information may serve to indicate appropriate fields for his clinical investigations. It will take him only a few weeks to learn, for example, that cerebrovascular disease is the commonest serious neurological disorder, or that the heredo-degenerative conditions which occupy so disproportionate an amount of space in the literature pale into numerical insignificance by comparison with the problem of disseminated sclerosis, of which every out-patient day yields two or three fresh cases. If he works amongst the maritime population of Liverpool he will remain familiar with the manifestations of neurosyphilis, steadily becoming both less common and less classical in type: in Newcastle this disease is so great a rarity that we stand in some danger of overlooking the occasional case of general paresis amongst the many patients who present with non-specific presenile dementias.

But, more than this, the provincial neurologist serves a relatively static population, and the universal coverage of the National Health Service has provided him with unequalled and as yet largely unexploited fields for long-term follow-up studies. The special hospital, with its episodic relationship with patients and its concentration on the serious or difficult case, may yield erroneous

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ideas about the natural history of a disease as it occurs in the general population. Such a difference must surely be responsible for the observation that in Newcastle, as in Leeds and Manchester, myasthenia gravis is most often a mild, chronic, remittent disorder, commonly undiagnosed for several years after the appearance of the first symptom, and in the large majority of instances adequately controlled by drugs, without recourse to the unpredictable hazard of thymectomy, so often necessarily invoked in the more serious cases encountered in the special hospital.

Acutely Ill Patients

A second, immediately noticeable, difference is that in the general as opposed to the special hospital the neurologist's patients are often acutely and sometimes catastrophically ill. Indeed, perhaps the commonest of all the problems the neurologist is asked to help his hospital colleagues to elucidate is that of the patient admitted unconscious—a differential diagnosis so simple in the textbook, but in fact comparable in difficulty only to that supreme test of diagnostic skill the acute abdomen. It is clear that topographical neurology affords little help in a problem of this nature, which emphasizes at once the truism that the neurologist in the general hospital must be a physician even before he is a neurologist. In this connexion I think one of our most humiliating experiences is the infrequency with which the neurologist can add anything of value to the elucidation of the common and baffling problem of the infant or young child comatose with an acute cerebral illness. The diagnostic problems posed by the comatose patient are indeed illimitable, but I will quote three brief cases in illustration of my point.

A 6-year-old child was admitted to hospital in a state of mental confusion. He had been vaguely off colour for a few days with symptoms described as "influenzal," and then he began to vomit. At the same time his behaviour became successively odd, curiously psychotic, and finally completely disorientated: within 24 hours a confusional state gave place to stupor and then to deep coma. An irregular fever was accompanied by intermittent generalized muscular twitching and by signs of left hemiparesis, without meningism or spinal fluid changes. A diagnosis of encephalitis, probably of post-infective type, had already been made. The only clue to the nature of the condition on examination was faint icterus, with a little bile in the urine, followed by a progressive decrease in liver dullness. Necropsy revealed an acute hepatitis as the only abnormal finding and the presumable cause of his cerebral illness.

A few years ago I published an account of a family in which three children had several episodes of encephalitic illness each arising in relation to apparently non-specific infections of the upper respiratory tract. More recently I thought I had encountered another such case, and it was only the combination of an astute paediatric registrar and a series of blood barbiturate estimations which revealed that the recurrent episodes of stupor in this case were in fact due to a psychopathic mother's repeated attempts to poison the child with her sleeping tablets.

In the history of a comatose woman of 30 admitted as a case of probable cerebral accident, the only significant feature was that for five years she took 4 pints (2.3 litres) of water to her bedroom every night, and drank them all by morning. Her blood urea was 450 mg./100 ml. and neropsy revealed a solitary aplastic kidney the size of a walnut, probably the result of a foetal nephritis.

Undiagnosable Cases

Since practically all the neurological material presenting at the general hospital is unselected it follows also that patients are often seen early in the development of their disease—often too early for the comfort of the neurologist. Most of the cases in our wards are definitely "membership" cases, and the florid physical signs which are the delight of the Conjoint candidate are strangely lacking in the provinces. Sometimes our cases are frankly undiagnosable. More often they resist the whole gamut of hospital investigation to declare themselves with the passage of months or years.

I have in mind a problem encountered in the children's department—the child who begins to walk abnormally. I refer not to the occasional very young child who, as she learns to walk, obstinately does so for a period of months on the toes of both feet with her heels raised. I have never heard any plausible explanation of this curious phenomenon, but it seems in most instances to demand little more than reassurance of the mother. I refer rather to the child of from 5 to 10 years old who starts to invert or plantarflex one foot while walking. At first this is intermittent; but gradually it persists, though even at this stage the child may occasionally be able to walk almost normally for a few minutes. The diagnosis of a missed poliomyelitic infection which has usually been made in such cases is negated by the firm or intermittent spasm which can be felt in the muscles involved. The patient has usually already resisted manipulation under anaesthesia, the application of a plaster splint, and psychiatric investigation. As over the months the gait becomes more bizarre, and inexplicable on any of the crude physiological bases with which we are familiar, it becomes indeed almost certain that the child will spend some time in the hands of a psychiatrist, and my own experience is that if the dread diagnosis of torsion spasm is made at all before the child is seen by a neurologist it is most often the psychiatrist who has made it.

To see cases too early is a mixed blessing, and affords less immediate satisfaction than the working out of the more fully developed problem as it often presents itself later in the special hospital.

A small girl was sent to me from a distance because, although her sole symptom had been two major epileptic fits, her electroencephalogram was so wildly abnormal that the psychiatrist who carried it out was suspicious of structural brain disease. When I saw her a week later the only abnormal physical signs were some very slight unsteadiness on her feet while dressing, which could not be elicited by formal testing, and a fine intermittent irregular tremor of her left hand made worse by willed movement. Despite the unusual onset, difficulty in deciding the nature of this involuntary movement immediately raised the suspicion of Wilson's disease, in which it is so often difficult to disentangle the striatal and the apparently cerebellar components of such tremors. There was indeed a strong suspicion of change in temperament and of early intellectual deterioration. The history, however, was short, there had been recent morning headache, and the child vomited as she was brought into the consulting-room. She was admitted to hospital at once, where full investigation with a view to the exclusion of tumour drew a complete blank, as did biochemical tests, which lent no support to the suspicion of hepato-lenticular degeneration. She was sent home undiagnosed, to return a fortnight later with acutely advancing cortical blindness bespeaking a diagnosis of Schilder's disease.

A Field for Clinical Investigation

To the neurologist working in a general hospital the nervous complications of established disease involving other systems of the body, often already under treatment by his medical and surgical colleagues, afford a major interest. That this is a fruitful field for clinical investigation needs no emphasis. It is necessary to refer only to recent studies of the flaccid ascending paralyses occasionally seen in renal disease, after ureteric transplantation, or during the treatment of diabetic coma, and to their dramatic relief by the administration of potassium salts; or to the striking episodic neuropsychiatric manifestations of chronic liver disease, so consistently associated with a raised blood ammonium level and preventable by restriction of protein intake. There are other examples of neurological illness based on functional and reversible humoral changes arising outside the nervous system, elucidation of which defies both neurological examination and the microscope of the neuropathologist, but yields to the techniques of the biochemical laboratory.

The ophthalmological, diabetic, and endocrine clinics are well-known mines of material for the neurologist, and this traffic is two-way. Experience in the clinical recognition of masked thyrotoxicosis is vital to the diagnosis of an appreciable proportion of cases of chronic ophthalmoplegia in middle-age, while Addison's disease may present as flaccid paraplegia. But there is scarcely a department of the hospital which has not something similar to offer.

Only close contact, for example, with a busy haematological clinic reveals the frequency in leukaemia of neurological complications due to infiltration, thrombosis, or haemorrhage. This disease may present with such signs as unilateral or bilateral exophthalmos, hemiplegia with or without papilloedema, an acute transverse lesion of the spinal cord, paralysis especially of the sixth or seventh cranial nerve, or subacute lesions of peripheral nerve trunks. Changes in the spinal fluid which are highly suggestive of infective meningitis may further confuse assessment.

Even the apparently banal cerebrovascular accident may depend on a critical aetiological event occurring outside the neuraxis, and on occasion outside the cardiovascular system.

A general practitioner taken acutely ill in his surgery was pale, confused, and disorientated. He was unable to understand simple questions, his speech was incoherent, and there was weakness of the right lower face without signs of paresis elsewhere. He was at this stage unable to give any history. The blood pressure was low and the case appeared to be one of cerebral thrombosis. However, within three hours of admission to hospital the neurological signs had completely disappeared, and at this time he was able to complain of mid-sternal pain. Examination revealed a rub over the praecordium, and electrocardiography confirmed the presence of a small posterior cardiac infarct.

The implication of some such major pathogenic factor is of course common in hypotensive vascular lesions of this kind. Sometimes the occurrence of a profuse haematemesis or melaena clarifies the pathogenesis in a confused or stuporous old man admitted with sudden hemiplegia. Less obvious was the case recently encountered of a woman of 39 in whom the deep stupor of a brain-stem infarction, still evident a month later in bilateral ptosis and hemianaesthesia, accompanied the exsanguination of a ruptured ectopic pregnancy.

Nervous Complications

The nervous complications of general diseases have, however, a special importance for the neurologist. We know much more about the aetiology and pathogenesis of general diseases than we do in the case of primarily neurological disorders, and on occasion the nature of pathological changes in the nervous system may be revealed only by considering the quality of such changes involving other parts of the body. The lessons of general pathology may be applicable to problems which are at first sight purely neurological.

One example will suffice. During the last twenty years neurologists have played a prominent part in describing the clinical and pathological features of polyarteritis nodosa. Meanwhile in a brilliant series of pathological and experimental observations Arnold Rich had demonstrated the identity of the changes observed in this disease with those seen in human and experimental serum sickness, and had afforded convincing evidence that, in many cases at any rate, polyarteritis represents a vascular manifestation of anaphylactic hypersensitivity to a variety of antigens. It had also been shown that the polyneuritis of this disorder, often symmetrical and indistinguishable in many instances from so-called "infective polyneuritis" of the Guillain–Barré type, is based not on vague "toxic" changes but on microscopic arteritic occlusions of the vasa nervorum. More recently it became clear that, like the fever, arthralgia, and abdominal pain of the disease, the peripheral neuritis of polyarteritis nodosa often responded strikingly to cortisone. The administration of this drug in cases of infective polyneuritis was an obvious step. The frequent and sometimes very dramatic therapeutic response encountered lends support to the view that the polyneuritic, like the myelitic and encephalitic, complications of acute infections are in all probability neurological manifestations of hypersensitivity mediated through the vascular tree—a view which has of course received further support from recent experimental observations.

Treatment

Another important difference worthy of attention is in the matter of treatment. The neurologist in the general hospital works as a member of a medical team, most members of which have at their command potent therapeutic agents ranging from hormones and antibiotics to such complex developments as the artificial kidney. He cannot feel entirely at ease in such company if his contribution is limited to the exercise of an ability to attach appropriate labels to rare, obscure, degenerative, and untreatable disorders, no matter how accurate his diagnoses. Much of the charge of therapeutic nihilism levelled at the neurologist is of course unjustified. One reason for what may appear to be a relative poverty of neurological medicine in the therapeutic field is that as soon as radical therapy is developed in the case of a neurological disorder its management not unnaturally ceases to be the exclusive preserve of a small group of specialists.

This trend to pass back from neurology into the realm of general medicine what has already been clarified is surely one to be welcomed: the special skills and opportunities of the neurologist are more profitably employed in the elucidation of unresolved problems at the growing edge of his subject. However, the rather unkind observation of a medical colleague that only three out of the last hundred papers published in *Brain* held out any hope for the patient is perhaps not entirely without significance. In fact, there have been two and a half papers in that journal devoted to treatment during the past three years, and two of these dealt with the not exactly day-to-day problem of the control of myotonia. It is difficult to rebut in its entirety the imputation that neurologists are not very interested in treatment, and one looks in vain through the current British literature of the subject for reports of those carefully controlled therapeutic trials which represent so characteristic and valuable a contribution to other fields of modern medicine. The researches of the neurologist in the general hospital may on occasion be hampered by the less highly developed technological services available to him, but for reasons outlined above he may well be in a very favourable position to initiate controlled investigations into scientific therapy.

Approach to Clinical Research

It is indeed a comparison of their approaches to clinical research which reveals the most significant difference between these two neurological orientations. Any such generalization immediately evokes the quotation of exceptions, but it is probably broadly true that the investigational work of the more highly differentiated physician whose main sphere of activity is the special hospital tends to draw its inspiration predominantly from neurophysiology, that of the general hospital neurologist from general medicine. The more specialized or academic physician in neurology, as in other branches of medicine, usually leans to the current view of clinical science which we owe to Sir Thomas Lewis and which finds its chief, and in some hands its exclusive, expression in the instrumental and laboratory investigation of clinical phenomena. Most such observations are devoted to the pathophysiology of symptoms, and the neurologist of this school tends to regard his investigations as a clinical pendant to those of the neurophysiologist. Such research is indeed often frankly directed towards elucidation of normal physiological mechanisms by the study of clinical lesions.

The research interests of the general hospital neurologist are usually more pragmatic. Constantly reminded that medicine was a useful art long before it tried to become a science, he remains more vitally concerned with the causes, management, and prevention of nervous diseases than in analysis of their intimate mechanisms. His conception of clinical science is catholic, leaning commonly towards the approach of the natural historian rather than to that of the experimental scientist.

Conclusion

It is indeed curious that the more restricted phenomenological view of clinical science enjoys at the moment so much more prestige than the traditional and broader biological concept which regards the natural history of disease in all its aspects as a valid subject for scientific inquiry. But these two approaches are, of course, complementary and in no

way mutually exclusive. What we term a disease is not an entity but a chain of interlinked events a few of which are faintly illumined here and there by the dim and flickering light of partial understanding. It is the physician's business to break this chain at some point along its course and thus free the patient from the inexorable development of his lesion. In this connexion recent vindications of the observational method, reinforced by the revolutionary contemporary techniques of statistics and epidemiology, are surely no less dramatic than the triumphs of the laboratory. The relation of maternal rubella to developmental defects, of cigarette-smoking to lung cancer, or of parity, sexual habits, and religion to carcinoma of the cervix uteri are contributions of basic biological significance, while by illuminating causation they point the way clearly to prevention and control.

Many such aetiological factors must lie buried in the histories of our neurological patients. But the weakest link in the chain is not always at its beginning, and the clinical scientist whose studies are devoted to mechanisms of symptom-production can justifiably point to many instances in which it is his investigations which have led to the effective control of disease by interrupting the pathogenetic sequence at some later stage in its course. After all, both alkalis and gastrectomy are more generally effective in the treatment of peptic ulcer than psycho-analysis, the initial lesion of diabetes mellitus remains veiled in mystery despite the adequate control of the disease which can be achieved with insulin, and modern anticonvulsant drugs will control many cases of epilepsy in the genesis of which the respective contributions of genetic and environmental factors remain at present entirely obscure.

LYMPHADENOID GOITRE (HASHIMOTO'S DISEASE)

A CLINICO-PATHOLOGICAL STUDY

BY

R. L. B. BEARE, M.B., B.S., F.R.C.S.

Lately Surgical Registrar, the Middlesex Hospital, London

Following the pioneer work of Roitt *et al.* (1956), the pre-operative diagnosis of lymphadenoid goitre may now be made with some precision. A series of cases is presented with a view to defining with like precision the histological features of the thyroid gland in this condition. At the same time the clinical features are described and the treatment and aetiology of the disease are discussed.

Present Series

The series consists of 33 cases of lymphadenoid goitre and represents all patients with this disease operated on at the Middlesex Hospital by the surgical staff over the last twenty years. It should be pointed out that the criteria on which inclusion in this series was based were strict; consequently a further 20 cases, whose claim to inclusion was the presence of lymphocytic infiltration in the thyroid gland, have been excluded. In addition a small number of patients not operated upon, but whose diagnosis has been confirmed and who have been treated medically, are discussed.

During the period 1935–55 2,141 thyroidectomies were done at the Middlesex Hospital, which represents an incidence of lymphadenoid goitre of 1.54%. Our impression is that this figure is too low and stems probably from the fact that most of these thyroidectomies were undertaken for toxic goitre.

In 1937 McClintock and Wright were able to identify a total of only 50 cases in the world literature, while Joll (1939) found an incidence of 0.9% in 5,650 thyroidectomies. More recently Heptinstall and Eastcott (1954) described an incidence of 2.7%. If the figures for thyroidectomy at the Middlesex Hospital be examined over the last five years the incidence of lymphadenoid goitre rises to 2.6% in 660 thyroidectomies.

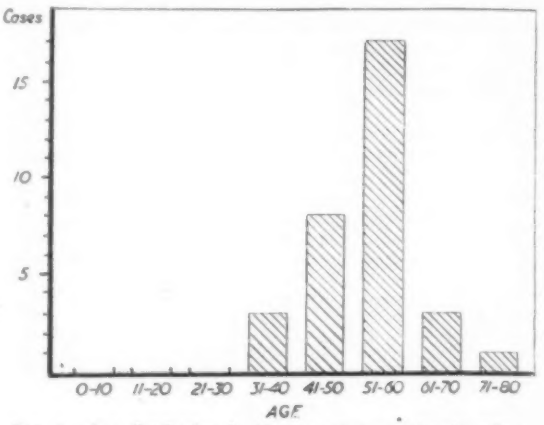

FIG. 1.—Age distribution in 32 cases of lymphadenoid goitre.

Age.—Lymphadenoid goitre characteristically affects middle-aged women. Our youngest patient was 37 years and the oldest 73, with an average of 51 years (Fig. 1). This age incidence agrees closely with that found by other authors. The disease may, however, rarely occur in childhood; for example, Statland *et al.* (1951) describe two cases in girls of 10 and 14 years, the latter having had a goitre since the age of 6.

Sex.—In all series described there is an overwhelming preponderance of female patients, the incidence being over 95%. We have only one example of lymphadenoid goitre occurring in the male, a doctor of 64. Likewise Marshall *et al.* (1948) describe only one male case in a series of 78 patients.

Symptoms

The Goitre.—A swelling in the neck has been noticed by the patient in all cases, but the duration of history varies widely from as little as one month in one case up to 35 years in another. However, the simple average in our cases is 2½ years; this is a fairly representative figure of the duration of the goitre before medical advice is sought. We have doubts, which are expressed below, whether the few patients who give a history of goitre of many years' duration have in fact had a lymphadenoid goitre during all that time.

Discomfort in Neck.—This is a common symptom, and appears to be a characteristic feature of the disease, occurring more commonly with lymphadenoid goitre than with colloid goitres of comparable or larger size. Over one-third of our patients complained of a feeling of discomfort and tightness in the neck, not amounting to pain but nevertheless a constant annoyance, particularly when lying prone. In only three cases was the *onset* of the goitre marked by definite pain in the neck, although seven patients had noticed pain and tenderness in the goitre at various times. Headache was not uncommon and was complained of by one-third of the patients.

Thyroid Deficiency.—Gross myxoedema is uncommon, but one-third of the patients volunteered the information that their voice had become hoarse, and this feature corresponds broadly with those who showed other signs of thyroid deficiency. In two such patients a recurrent laryngeal nerve palsy was suspected, but laryngoscopy demonstrated only

thickening of the vocal cords with a full range of movement. Lassitude is a common complaint, and a change in weight, usually but not necessarily a gain, was mentioned by 10 out of our 33 patients.

Pressure Symptoms.—Major effects due to pressure by the goitre are rare, but minor degrees of *dysphagia* are not uncommon, being manifested as a discomfort on swallowing rather than by any hold-up. In one patient the goitre was largely intrathoracic, and she complained of severe choking and breathlessness, especially on lying down. *Breathlessness* is an uncommon complaint, although moderate degrees of tracheal deviation and narrowing are often seen on the *x*-ray films. *Venous obstruction* is sometimes present, and occurred in three patients in this series. A useful test for unmasking early venous obstruction may be carried out in the following way. The patient is asked to hold the arms above the head; the change of posture at the thoracic inlet may then result in immediate and visible engorgement of the external jugular veins, together with congestion, flushing, and even swelling of the face if the obstruction is severe. One such patient volunteered the information that she had suffered flushing and swelling of the face, often followed by a headache, whenever she raised her arms to comb her hair.

A characteristic but inexplicable feature of the disease is the way in which all the symptoms tend to fluctuate in intensity and to vary from time to time.

Examination of the Goitre

The goitre itself is usually firm and symmetrical, with an average weight of about 100 g. As Joll (1939) points out, the enlargement affects every part of the gland, and any asymmetry is presumably due to pre-existing asymmetry of the thyroid. The pyramidal lobe invariably takes part in the enlargement when it is present, and is readily palpable, sometimes the effect being that of a trilobed goitre. The amount of fibrous tissue in these goitres varies, and so, therefore, does their consistence on palpation, a few being hard enough to suggest malignant disease. The fibrosis is responsible, when pronounced, for the characteristic bosselation of the gland surface. The enlarging lateral lobes push the carotid arteries backwards and laterally, where they may be palpated; and not infrequently these lobes pass behind the oesophagus to meet one another in the midline, forming the so-called "ring" or circular goitre. The gland moves freely on swallowing except in so far as it may be hampered by its size or shape.

Assessment of Thyroid Function

Most patients with lymphadenoid goitre have a depressed thyroid function. This amounts to frank myxoedema in about one-fifth of the cases. Of the remainder one-half can be clinically suspected of hypothyroidism, while the others are apparently in an euthyroid state.

It should be mentioned that some patients have clinical features which may lead the unwary to an erroneous diagnosis of thyrotoxicosis. Symptoms such as loss of weight, irritability, and tremor are sometimes described by the patient, but objective signs of thyrotoxicosis are lacking, with a normal pulse rate and cool hands. It should be remembered that the hypothyroid patient may be as irritable as her thyrotoxic neighbour, and that a depressed thyroid function may, by depressing appetite, particularly in the early stages, engender loss of weight.

Laboratory Investigation

Basal Metabolic Rate.—This is usually lowered or is at the lower limit of normal. For reasons discussed below we do not hold the view that lymphadenoid goitre *cannot* follow thyrotoxicosis, though it apparently rarely does so: in such a case the B.M.R. may be estimated at a time when it is falling from the hyperthyroid to the hypothyroid range (an inevitable result of the lymphadenoid reaction) and so be found still raised above the normal. In this series the B.M.R. was determined pre-operatively in 24 patients. The Robertson–Reid scale, with a stated normal range of −15% to +15% has been used at this hospital for the past five years. The B.M.R.s of 10 patients whose rates were determined on the Robertson–Reid scale have been converted to the Aub–Du Bois standard (Fig. 2), which was in use prior to 1952.

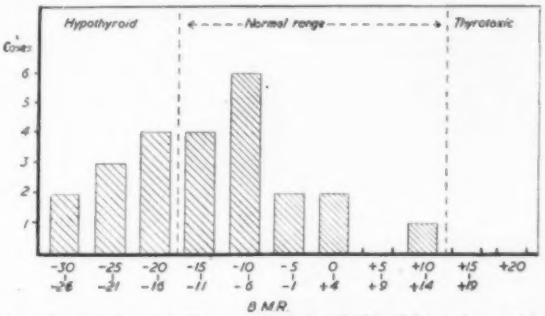

FIG. 2.—Basal metabolic rates (Aub–Du Bois) of 24 patients with lymphadenoid goitre.

Serum Cholesterol.—This is a poor index of thyroid function, but, in the absence of concomitant conditions such as pregnancy, diabetes, renal failure, severe anaemia, etc., may be used as a rough test for myxoedema, being a less tedious, though less accurate, assessment of thyroid function than the B.M.R. The serum cholesterol was determined before operation in eight patients in this series. The values ranged from 156 to 380 mg./100 ml., four of the eight lying above the normal range (150 to 250 mg./100 ml.).

Radioactive Iodine Studies

Radioactive iodine investigation has been carried out on eight patients in this series. The results show a considerable uniformity. In most cases the 24-hour uptake level in the gland is raised to about 50% of the dose administered (Table I), a level which is generally regarded as lying at the upper end of the normal range or within the lower range of overlap with toxicity. The probable explanation of this paradox is discussed below.

TABLE I.—*Radioactive Iodine Studies in Eight Patients With Lymphadenoid Goitre, Showing 24-Hour Uptake as a Percentage of Test Dose*

Case No.	Uptake	Case No.	Uptake
13	50·4%	22	35%
14	48%	31	57%
20	60%	32	52%
21	33%	33	42·4%

Urinary excretion figures are complementary to the high uptake and lie in the region of 30%.

The topographical surveys showed isodose curves evenly distributed over the goitre, corresponding accurately with the palpable enlargement; and indeed we regard a localized uptake or absence of uptake from a major part of the goitre as evidence against a diagnosis of lymphadenoid goitre (Figs. 3 and 4).

The 48-hour plasma radioactivity was determined in one patient (Case 32). The protein-bound fraction was found to be 0.66% of the administered dose per litre of serum, a figure which lies unequivocally in the toxic range (Silver *et al.*, 1955). However, clinically she was *hypothyroid*, with a B.M.R. of −25%.

The probable explanation of this apparent paradox and also of the slightly raised 24-hour uptake in the gland depends on the level of the thyroidal iodine pool, which is known to be low (Skillern *et al.*, 1956). The administered test dose of ^{131}I represents, therefore, a larger proportion of the iodine which is available for synthesis of thyroglobulin than in the normal or thyrotoxic gland. Consequently a larger proportion of the circulating thyroid hormones will

be labelled with ^{131}I. This is probably not the only explanation of these phenomena, and it seems likely that overactivity of pituitary T.S.H. also plays a part.

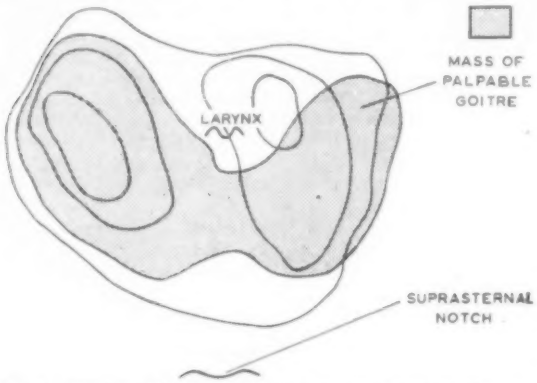

FIG. 3.—Topographical survey of Case 20 with outline of palpable goitre superimposed on isodose curves.

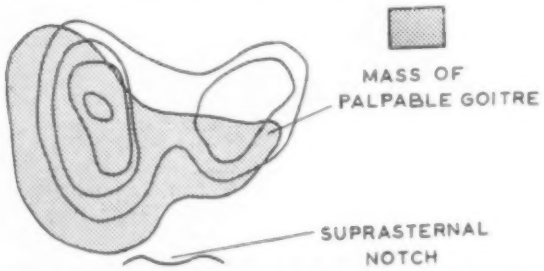

FIG. 4.—Topographical survey of Case 33 with outline of palpable goitre superimposed on isodose curves.

Precipitin Reaction and Other Tests

Though still in an experimental stage, the precipitin reaction is now being developed as a specific test for lymphadenoid goitre. Roitt *et al.* (1956) have shown in a preliminary communication that the serum of patients with lymphadenoid goitre contains a circulating antibody which will give a precipitin reaction with thyroglobulin as the antigen. The test has been performed in only three cases in this series, all showing a strongly positive result.

Other tests, less specific than the precipitin reaction, which reflect, nevertheless, the presence of a raised γ-globulin, and which may provide contributory or even diagnostic evidence, are:

1. *Plasma Protein Electrophoresis.*—The electrophoretic pattern demonstrates the presence of a raised γ-globulin level (Figs. 5 and 6).

2. *Flocculation Tests.*—The flocculation tests (thymol turbidity, zinc sulphate, and colloidal gold) show high values reflecting the alteration in the plasma protein, and typical results in four cases were (units):—*Case 1:* thymol turbidity, 9; zinc sulphate, 21. *Case 32:* thymol turbidity, 15; zinc sulphate, 19; colloidal gold, 5. *Case 33:* thymol turbidity, 12; zinc sulphate, 29; colloidal gold, 5. *Case 13:* thymol turbidity, 10; zinc sulphate, 12; colloidal gold, 4. (*Normal values:* thymol turbidity, 0–4 units; colloidal gold, 0–1 unit; zinc sulphate, 0–12 units.) Even if facilities for protein electrophoresis are not available the finding of abnormal flocculation tests in a hypothyroid woman with a firm symmetrical goitre is almost diagnostic of lymphadenoid goitre.

3. *Erythrocyte Sedimentation Rate.*—This is usually raised in patients with lymphadenoid goitre. However, it is so non-specific as to be of little value as a diagnostic test. Its interest lies in the fact that the raised E.S.R. is due to the presence of the abnormal γ-globulin, and it was the E.S.R. which provided the first clue which led Roitt *et al.* (1956) to the discovery of the antigen–antibody (precipitin) reaction. Nevertheless a raised E.S.R. may be of some help in diagnosis when biochemical facilities are not available, and, conversely, we believe that a normal E.S.R. is evidence against a diagnosis of lymphadenoid goitre. The E.S.R. was determined pre-operatively in eight of our cases (Table II).

TABLE II.—*E.S.R. (Wintrobe—correct to P.C.V. 45%) (Normal 0–10 mm.)*

Case No.			Case No.			Case No.		
1	..	16 mm.	20	..	58 mm.	31	..	39 mm.
6	..	38 ,,	22	..	27 ,,	33	..	77 ,,
13	..	40 ,,	30	..	15 ,,			

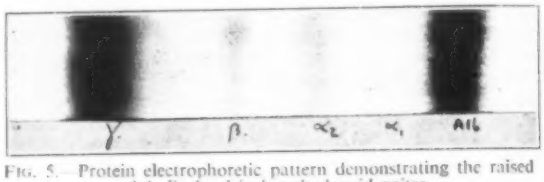

FIG. 5.—Protein electrophoretic pattern demonstrating the raised γ-globulin level in lymphadenoid goitre.

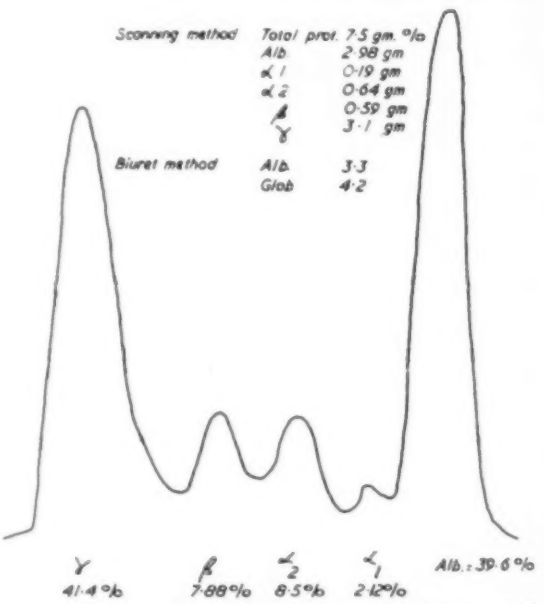

FIG. 6.—Protein electrophoretic tracing demonstrating the raised γ-globulin level in lymphadenoid goitre.

Radiological Examination

Plain *x*-ray films of the thoracic inlet demonstrate that minor degrees of tracheal deviation and compression occur commonly. Radiological studies were carried out in 25 of our patients, and 15 of them showed tracheal deviation or compression. In three of these the airway appeared sufficiently obstructed radiologically to provide the reason for operation. Retro-oesophageal extension of the goitre, with mild distortion of the oesophagus on barium swallow, was seen in three patients. In only one patient was there a true intrathoracic extension of the goitre.

Reasons for Operation

(1) *Suspected Malignancy* (11 cases).—This was the most frequent reason for operation, and arose particularly when the goitre was of short duration or had increased rapidly in size of recent months. The occasional real hardness of

the gland, as opposed to mere firmness, was another factor leading to a suspicion of cancer. In addition three cases showed marked clinical enlargement of the regional lymph nodes; so great was this enlargement in one case, which showed a chain of firm, rubbery glands extending up to the angle of the jaw on one side, that a block dissection of the neck was carried out at the same time as the thyroidectomy. Section of these glands showed non-specific reactive hyperplasia only. (2) *Pressure:* on trachea in 6 cases, on oesophagus in 2, on veins in 2. (3) *Cosmetic:* 3 cases had large ugly goitres. (4) *Discomfort in neck:* 3 cases. (5) *Pain in neck:* 2 cases. (6) *Diagnosed as thyrotoxicosis:* 1 case. (7) *Undetermined:* 9 cases.

Treatment

Thyroid Extract.—Evidence is accumulating to show that lymphadenoid goitre can be effectively treated by the administration of thyroid by mouth. Thus Heptinstall and Eastcott (1954) comment on the improvement which may follow the administration of thyroid to these patients. Statland *et al.* (1951) remark on the efficacy of thyroid in preventing regrowth of lymphadenoid goitre after operation and consider that it may be a useful form of primary treatment. They describe two cases in which goitres resolved completely on thyroid treatment, following a biopsy which confirmed the diagnosis. Six patients in our present series received pre-operative treatment with thyroid extract in doses varying from ½ to 2 gr. (32 to 130 mg.) daily. In only two of these was medication sufficiently prolonged or in dosage high enough to constitute a genuine attempt at treatment with thyroid extract. The results are interesting (Table III).

TABLE III

Case	Medication	Results
13	2 gr. (130 mg.) daily ? time	Voice became clear; gland smaller and softer; pain in neck relieved
14	1 gr. (65 mg.) daily for 6 months	Some resolution in size of gland
19	1 gr. (65 mg.) daily ? time	Gland became smaller
23	½ gr. (32 mg.) daily for 1 month	Gland became softer
32	2–3 gr. (130–200 mg.) daily	Goitre became much smaller and neck circumference fell from 14½ to 12 in. (30 to 37 cm.) in six weeks
33	1 gr. (65 mg.) daily	Patient failed to co-operate in treatment

Cases 13 and 32, who received 2 gr. (130 mg.) of thyroid daily, responded very favourably to treatment. It may be asked, therefore, why they were operated upon. However, in Case 13 the goitre was large, and it was not then appreciated that treatment with thyroid extract, in order to prove effective, must be continued for many months. Case 32 was a psychoneurotic patient who would take her thyroid tablets only in spasmodic and brief bouts in enthusiasm.

During the last two years I have been associated with Vaughan Hudson and Doniach in the treatment of four patients with lymphadenoid goitre who have been relieved of their symptoms and whose goitres have become impalpable on the daily administration of 2–3 gr. (130–200 mg.) of thyroid extract.

Radiotherapy.—Many workers have advocated radiotherapy in the treatment of lymphadenoid goitre (Crile, 1948; Schilling, 1945). There is no doubt that irradiation will bring about a diminution in the size of the gland, mainly by its effect on the lymphoid tissue. However, in view of the apparent efficacy of thyroid treatment and the precision with which the diagnosis can now be made, we do not regard radiotherapy as the treatment of choice in this condition.

Surgery.—In 1939 Joll wrote: "It is a matter of considerable doubt as to whether surgical treatment is necessary in Hashimoto's disease, assuming that pressure symptoms are slight." This statement is more than ever true to-day. Nevertheless there are circumstances in which surgical intervention must be seriously considered, especially in the following conditions. (*a*) In the presence of major pressure symptoms which demand rapid relief, particularly should the goitre be partly intrathoracic. (*b*) When the diagnosis remains in doubt, and the possibility of malignant disease is still present. Few tests give 100% precise results, and cases of lymphadenoid goitre are known (Doniach, 1957, personal communication) in which the antibody titre is too low to be detected by the precipitin reaction in its present form. Furthermore, as described under the heading "Pathological Features," occasionally these goitres are accompanied by a massive lymph-node enlargement, such as would render a diagnosis of lymphadenoid goitre by biochemical methods unacceptable until the neck had been explored. (*c*) Failed medical treatment: it is likely that some lymphadenoid goitres will fail to respond satisfactorily or rapidly enough to medication with thyroid extract. Lack of co-operation by the patient is another cause of failure.

The Operation

Little need be said of the technique employed. No difficulty is found in delivering the relatively avascular gland from its bed, though occasionally the characteristic retro-oesophageal extension may prove troublesome, and the operation, in the absence of venous obstruction, is unusually bloodless.

The aim should be to perform a subtotal thyroidectomy rather than the conservative resection sometimes recommended. It is felt that recurrence, though uncommon, is less likely after the subtotal operation; and Ficarra (1946) believes that recurrence is always due to inadequate surgical removal. However, Statland *et al.* (1951) have shown convincingly that regrowth of the goitre is seen only in those patients who fail to take thyroid post-operatively.

It seems possible, therefore, that recurrences after the conservative excision may arise because the surgeon mistakenly considers that he has left the patient with a reasonable amount of functioning thyroid tissue. For this reason the patient may receive no thyroid, or inadequate doses thereof, after operation, and consequently the goitre recurs. It must be emphasized that the myxoedema of greater or less degree is the inevitable result of lymphadenoid goitre; surgical excision of the gland, whether partial or subtotal, hastens the onset of this state and necessitates the supply by mouth of the patient's total requirement of thyroxine.

Care should be taken to excise a pyramidal lobe, if present, and the parathyroids must be sought and safeguarded. If these are not found (and they may be particularly difficult to identify on the pale lobulated surface of the lymphadenoid gland) the "lateral leaf" of the thyroid remnant should be made thin, but longer than usual, the resection starting further forward on the surface of the lateral lobe than is usual.

Hemithyroidectomy, even when the contralateral lobe appears normal, should play no part in the surgery of lymphadenoid goitre unless the surgeon accepts the need for full post-operative thyroid medication. If this is omitted, or the need for it is not recognized, then enlargement of the remaining lobe is inevitable.

Pathological Features

The thyroid glands of the 33 patients forming this series all conformed to a similar pathological pattern, and the constancy of the cellular changes, regardless of the clinical size or length of history of the goitre, was a notable feature.

The weights of the thyroid glands varied from 50 to 350 g., with an average of 111 g. The gross appearance shows a diffuse enlargement of the thyroid which almost always involves both lateral lobes and the isthmus. The external surface of the gland shows lobulation, but the capsular surface remains intact to leave a glistening surface.

On cross-section the enlarged thyroids were replaced by pink or white homogeneous tissue involving almost all areas (Fig. 7), although a few colloid foci were discernible in some.

FIG. 7.—Showing the replacement of all lobes of the thyroid gland by white tissue (posterior view with the cleft for trachea).

Histology

The histological features are most readily described under the following headings.

Thyroid Epithelium.—There is no normal thyroid tissue in Hashimoto's disease. The thyroid epithelium shows degenerative changes, with lack of colloid production and disruption of many of the thyroid acini. The residual thyroid cells show a characteristic alteration (Ascanazi) in their cytology, with an increase in their size due to enlargement of the cytoplasm, which stains a prominent pink colour with eosin staining, while the nuclei are vesicular in appearance. These abnormal epithelial cells either occur in clusters or are sparsely scattered among the cellular infiltrate (Figs. 8 and 10).

Cellular Infiltrate and Lymphoid Follicles.—In all examples lymphoid follicles are present and form one of the diagnostic characteristics of this type of goitre (Figs. 8 and 9). The follicles are of variable size and shape, with a central pale staining area of cells surrounded by a rim of lymphocytes. These lymphoid follicles are indistinguishable from the lymphoid aggregations found elsewhere in the body. Apart from these focal follicular formations there is a diffuse cellular infiltrate in all examples, which permeate around groups and between individual cells of the residual degenerate thyroid epithelium. This cellular infiltration is composed predominantly of two types of cell, the lymphocyte and the plasma cell. The lymphocytes are maximal in number in the areas adjacent to the lymphoid follicles, but are also present in variable numbers throughout these pathological glands. In every example plasma cells formed a constant component of the diffuse cellular infiltrate, and in more than half the cases they exceeded the lymphocytes in number (Fig. 10). These plasma cells infiltrate diffusely throughout the gland, but in areas where the thyroid epithelium has disappeared the plasma cells form confluent foci. In a few examples polymorphonuclear leucocytes were present, but they were never prominent and were always outnumbered by lymphocytes and plasma cells.

Giant Cells.—These are present in many cases. They are of two differing types; one is the large multinucleate giant cell formed by aggregation of the altered epithelial cells; in other cases giant cells of the foreign body or even Langhans type are present, surrounding residual colloid material. These giant cells appear to be formed as a reaction to this colloid (Fig. 9).

Fibrosis.—Increased fibrosis of the gland forms a constant feature of these goitres. The glands are encapsulated by a thin band of fibrous tissue, and similar fibrosis subdivides the goitre into lobules, while coarser areas of fibrosis are present in the sites of advanced epithelial degeneration. A few examples show more extensive sheets of fibrous tissue permeated by inflammatory cells, but at no point was penetration of the capsule observed and the pathological condition always remained within the gland.

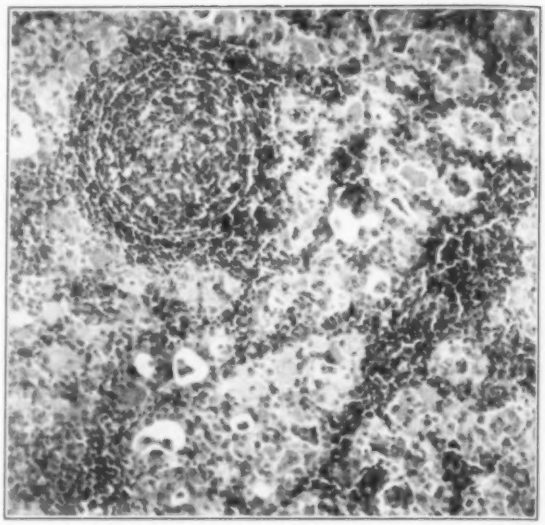

FIG. 8.—Showing a lymphoid follicle with diffuse cellular infiltrate permeating the residual thyroid epithelium. (×120.)

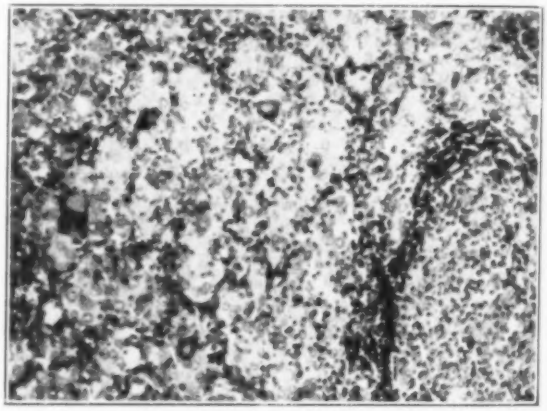

FIG. 9.—Showing a lymphoid follicle and giant cells in the thyroid epithelium in lymphadenoid goitre. (×142.)

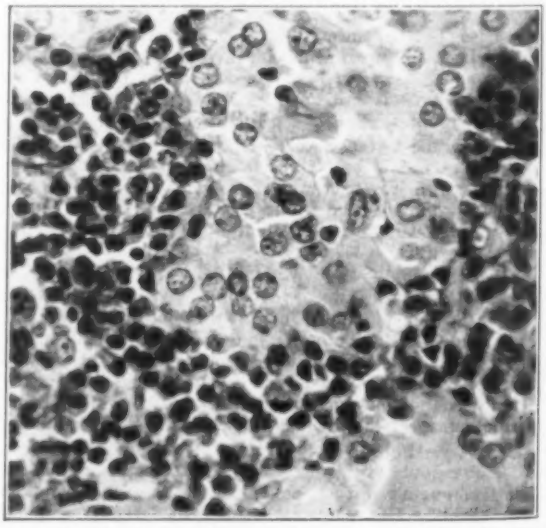

FIG. 10.—Showing lymphocytes and plasma cells infiltrating the residual thyroid epithelium. (×520.)

Regional Lymph Nodes.—A few cases showed marked enlargement of the cervical lymph nodes in addition to the goitre. In three examples of this lymphadenopathy was so marked that metastatic carcinoma was suspected. Histologically the enlargement of the lymph nodes was due to non-specific reactive hyperplasia.

Carcinoma and Lymphadenoid Goitre.—One case showed enlargement of the thyroid gland due to the cellular changes of lymphadenoid goitre, but in addition there was an area of primary carcinoma in the adjacent thyroid tissue (Fig. 11).

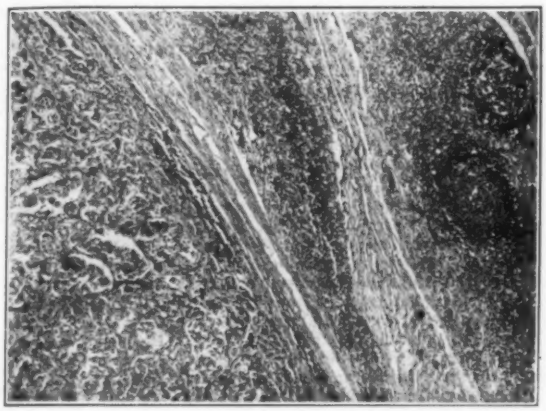

FIG. 11.—Showing a carcinoma of the thyroid with a lymphadenoid picture in the adjacent thyroid tissue. (×63.)

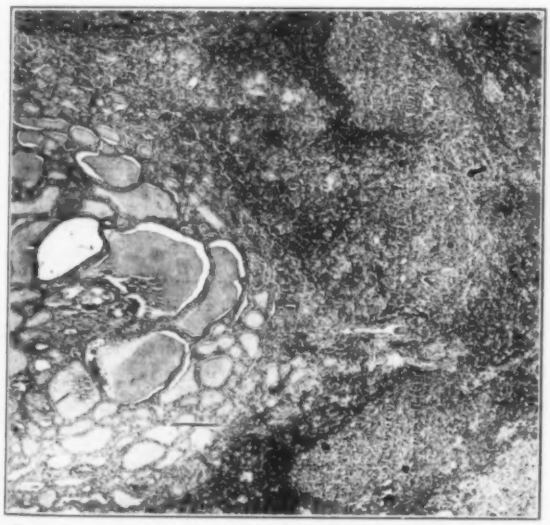

FIG. 12.—Showing a colloid goitre with an adjacent area of lymphadenoid tissue. (×50.)

Residual Colloid.—In three cases small areas characteristic of colloid goitre were observed. It is significant that these patients gave a history of goitre extending over 30 years, and it seems a reasonable assumption that in these the lymphadenoid reaction had occurred in a thyroid gland already the site of a colloid goitre (Fig. 12).

The Follow-up

It has already been stressed that the overwhelming majority of patients who have undergone thyroidectomy for lymphadenoid goitre will require full thyroid medication *for the rest of their lives.* The necessary maintenance dose varies with individuals, but the majority require between 2 and 3 gr. (130 and 200 mg.) daily of thyroid extract. This is also the order of dosage required to bring about resolution of a lymphadenoid goitre.

After operation the onset of myxoedema is inevitable and rapid. One of our patients (Case 13), who had been away to a convalescent home after thyroidectomy, delayed her first attendance in the out-patient department until five weeks after her operation. She had in this time already become so grossly myxoedematous that she was immediately readmitted to hospital for stabilization.

Another patient (Case 7), who underwent thyroidectomy for a large retro-oesophageal lymphadenoid goitre in 1948, lost touch with her family doctor and neglected to take her thyroid pills. She died in myxoedema coma in 1954.

Discussion

The curiously constant yet unusual type of tissue response in the lymphadenoid goitre lends itself to wide speculation on the precise causation of the disease process. Thus at various times the following suggestions have all been put forward as aetiological factors in lymphadenoid goitre: inflammation (Ewing, 1928), vitamin deficiency (McCarrison, 1929), functional disorder of colloid storage and release (Hellwig, 1938), subnormal thyroid tissue with compensatory lymphoid hyperplasia (Williamson and Pearse, 1925).

Levitt (1952) and others have regarded the disease as a waning hyperplasia, with progression toward thyroid fibrosis. However, it can be stated that the histology of the gland has contributed little to the solution of the aetiological puzzle, since the cellular appearances are compatible with most of the suggested causes.

The discovery by Roitt *et al.* (1956) of the presence, in the serum of patients with lymphadenoid goitre, of an antibody to the patient's own thyroglobulin suggests that the pathological changes in the gland itself are the results of an antigen–antibody reaction occurring locally, and that the cellular infiltration is secondary to this.

What remains obscure is the nature of the process which engenders this auto-sensitization. The preponderance of women in all series of lymphadenoid goitre suggests a possible linkage with pregnancy; however, no such connexion has been found, and, in any event, some other explanation would be needed of the few cases occurring in males and in children. Again, a rapid survey has failed to show any correlation between rhesus groups and this disease.

One interesting fact, however, has emerged from a study of the past medical histories in this series of patients. Previous histories were available in 27 cases, and a considerable proportion gave an antecedent history of diseases, the common denominator of which may be regarded as a pathological sensitivity on the part of the body tissues to various stimuli: thus rheumatic fever in 5 patients, rheumatoid arthritis in 3, nephritis in 2, and skin allergy in 4. In addition many gave a history of recurrent tonsillar infection, though this feature was too ill-documented to be of statistical value.

An interesting history of the onset of her goitre is given by one patient (Case 31). She had severe stomatitis following the extraction of some septic teeth: the goitre appeared suddenly, with considerable pain and tenderness of the gland itself, during the course of the stomatitis.

One may wonder, therefore, whether streptococcal infection with an allergic response may be in any way involved in this disease process. This is not suggested as a concrete theory, but merely put forward as a line for further study. We find no evidence to suggest, as Eason (1928), Vaux (1938), Levitt (1952), and others consider, that the lymphadenoid gland necessarily represents a late stage of thyrotoxicosis. On the other hand, if, as the serological evidence appears to show, the histological changes are the result of an antigen–antibody reaction taking place in the thyroid gland of a patient who has developed an auto-antibody to her own thyroglobulin, then there is no reason why such a change should not occur in the thyrotoxic patient as well as in the normal. Indeed, thyroglobulin extracted from toxic goitres

is just as satisfactory an antigen for use in the precipitin reaction as is that obtained from normal thyroids (Roitt *et al.*, 1956).

I have notes of one patient, aged 66 (Case 11), who was confidently diagnosed as thyrotoxic. The laboratory evidence did little to support this diagnosis, the B.M.R. being +13% (Aub–Du Bois). She was prepared with iodine, the B.M.R. fell to −1%, and a thyroidectomy was performed. Section of the excised gland showed a typical lymphadenoid picture. It is possible that this may have been an example of lymphadenoid reaction affecting a previously toxic gland.

It seems likely that the lymphadenoid change occurs independently of any pre-existing disease in the gland itself and, once engendered, will graft itself on whatever type of thyroid gland the patient already has. Thus, as would statistically be expected, most thyroids prior to being overtaken by the lymphadenoid change are normal. Sometimes, however, the patient already has a colloid goitre, and in Fig. 12 we illustrate a section of a typical lymphadenoid goitre in which are seen unmistakable traces of a colloid goitre. A few patients with lymphadenoid goitre give an exceptionally long history, usually terminated by a more rapid enlargement: it seems probable that these long-standing goitres have for many years been colloid in nature before being affected by the lymphadenoid reaction.

Likewise the change may affect the malignant gland, and Fig. 11 shows a carcinoma of the thyroid lying in the lymphadenoid gland. We have no evidence to suggest that malignant thyroid epithelium can or cannot be attacked by the lymphadenoid process. The carcinoma illustrated appears to be quite unaffected. Such a reaction, if it occurred, would presumably be linked to the ability of the malignant epithelial cells to elaborate thyroglobulin.

It seems, therefore, that this sensitization of the patient to her own thyroglobulin occurs as an episode in the life history of her thyroid gland: the histological changes are then imposed on the normal thyroid gland or on the toxic, colloid, or neoplastic goitre.

The lymphadenoid reaction may sometimes, I believe, be so overwhelming and complete that no functional thyroid tissue survives and the gland becomes a fibrous remnant; this may be the explanation of some cases of so-called primary myxoedema, a view already expressed by Statland *et al.* (1951). In support of this theory, Doniach (personal communication, 1957) has found a positive precipitin reaction in two such patients.

Summary

Thirty-three cases of lymphadenoid goitre are presented. Based on this material, the clinical features, diagnosis, pathology, and treatment are described, and in addition the modern concept of the aetiology is discussed.

The clinical features of our cases differ little from those so ably described by Joll (1939). All patients are either euthyroid or hypothyroid, with a 95% female distribution. Symptoms are discussed under the headings of thyroid deficiency, pressure, and the goitre.

Radiologically, major tracheal or oesophageal pressure is rare; minor degrees of pressure are common.

The laboratory investigations which are discussed include the B.M.R., radioactive iodine studies, and the precipitin (antigen–antibody) reaction described by Roitt *et al.* (1956). The value and significance of less specific tests such as plasma protein electrophoresis are discussed.

Treatment should be by the oral administration of thyroid extract, though the need for surgical excision will probably arise in certain circumstances, notably for the urgent relief of pressure and for the establishment of the diagnosis. After thyroidectomy, myxoedema and/or recurrence of the goitre will follow if the need for continued thyroid replacement is not recognized. The need for careful follow-up of both medically and surgically treated cases is emphasized.

The pathological features of the lymphadenoid gland are described and attention is drawn to the high proportion of plasma cells present in the diffuse cellular infiltrate.

Histological evidence is presented which supports the view that while the lymphadenoid reaction usually affects a thyroid gland which was previously normal this is not necessarily so; colloid goitres, thyrotoxic goitres, and malignant goitres may, it is believed, be so affected.

The immediate cause of the lymphadenoid change appears to be the result of an auto-sensitization to the patient's own thyroglobulin.

The underlying cause of this phenomenon is unknown.

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The Standing Technical Committee on Synthetic Detergents, appointed a year ago by the Minister of Housing and Local Government, has issued a progress report (H.M.S.O., London, price 6d. net). Foam occurring on rivers, canals, and sewage works remains a common cause of complaint. In some places the foam is so extensive and deep as greatly to reduce the chances of rescuing anyone falling into the water. At such places anti-foaming agents are a necessary concomitant of lifebelts. The remedies used at sewage works against foaming are palliatives rather than cures, and manufacturers are investigating the production of synthetic detergents more readily decomposed at sewage works. The committee is also sponsoring research on this and similar problems. After the very rapid increase in the use of detergents between 1949 and 1954, the limit of consumption now appears to have been reached, or nearly so: in 1956 34,500 tons were used for domestic and 6,500 tons for industrial purposes.

STOSSTHERAPY IN ACUTE RESPIRATORY INFECTION IN CHILDREN

BY

M. C. JOSEPH, M.D., M.R.C.P., D.C.H.

Assistant to the Director of the Department of Child Health, Guy's Hospital, London

Stosstherapy was the name given by Harnapp (1938) to the method of treatment of rickets with a single massive dose of one million units of vitamin D. Later, Gaisford (1951) used the name to describe the single massive dose of sulphonamide which he used in the treatment of pneumonia and other infections. In Denmark and America this method of treatment has been called "shock dose."

Although stosstherapy is a relatively new method of treatment, Ehrlich (1913) was well aware of the advantages of cure by a massive single dose, the *therapia sterilisans magna*: "We must give strong doses, according to the maxim *Frapper fort et frapper vite*." In fact, Ehrlich had some success with stosstherapy, for a 300-bedded hospital in Surinam, used solely for the treatment of yaws, was emptied.

The first published report of stosstherapy in the treatment of respiratory infection in children was by Platt (1940). He used sulphapyridine in a single dose of 0.3 g. per kg., up to a maximum of 4 g. Patients treated during the same period with multiple doses formed a control group. He reported good and comparable results in the two groups. Since then other reports of satisfactory results from stosstherapy have followed (Karelitz and Weinstein, 1940; Vollmer *et al.*, 1944; Lauria, 1947; Wilken-Jensen, 1948; Friderichsen and Walther, 1950). The last-mentioned authors began using stosstherapy in 1941; from 1944 they used sulphathiazole instead of sulphapyridine, and after 1946 for 39 children they used penicillin in addition to sulphathiazole. By 1949 they had treated 1,500 children by stosstherapy. 875 of their patients had pneumonia, 90 lobar and 785 bronchopneumonia, of which 280 occurred in infants under 1 year of age. The case fatality for the 875 children with pneumonia was 4.9%. Jersild *et al.* (1956) treated 245 children with pneumonia with a single dose of 200,000 to 400,000 units of procaine penicillin, and compared the results with 323 cases of pneumonia treated with injections of procaine penicillin twice daily for five days; the single dose was as effective as the five-day course.

Material and Methods

The object of the present article was to compare the results of stosstherapy in acute lower respiratory infection in children with those of standard continuous chemotherapy. Between October, 1952, and October, 1954, 174 children with acute lower respiratory infection were admitted to the Evelina Children's Hospital of Guy's Hospital, and were treated with penicillin by injection or oral sulphonamide, or a combination of both. Sixty of these were treated by stosstherapy and 114 by a conventional continuous course of chemotherapy.

It was necessary to exclude certain patients from both treatment groups. From the stoss group of 60, 8 children were excluded (2, hilar adenitis; 1, whooping-cough; 1, mongol; 1, staphylococcal pneumonia; 1, middle-lobe collapse; 1, treatment delayed 16 days; 1, bronchiectasis). From the standard group of 114, 60 children were excluded (41, duration of penicillin less than five days; 10, treated with sulphonamide only; 5, chest films mislaid; 1, aged 2 weeks; 1, fibrocysic disease of the pancreas; 1, death within one hour of admission; 1, agammaglobinaemia). After these exclusions there remained for the present study 52 children in the stoss group and 54 in the standard group.

The method of treatment (stoss or standard) to be given was chosen by any one of fourteen doctors who admitted the patients and whose personal preferences dictated his decision.

The grouping of patients who clinically appear to have an acute infection of the lower respiratory tract is not easy, whether aetiological or anatomical classification is attempted. For simplicity in this article, the patients who clinically had an acute infection of the lower respiratory tract were grouped by radiological appearances: group 1a, consolidation confined to bronchopulmonary segments; group 1b, consolidation confined to whole lobe; group 2, consolidation not confined to bronchopulmonary segments, (*a*) discrete, (*b*) confluent; group 3, no radiological changes.

Comparability of the Two Treatment Groups.—Table I shows that the two groups on admission were similar in respect of clinical and radiological grouping, age, sex, number severely ill, and mean pulse rate. Patients in the stoss group differed from those in the standard group in the following respects: the average duration of illness before admission was shorter; more had a previous history of acute lower respiratory infection; fewer had been given immediate previous chemotherapy; the mean temperature on admission was higher in those patients in whom the temperature was recorded by the oral route—that is, the older children—and lower in those in whom the temperature was recorded by the rectal route; the mean respiratory rate on admission was lower; the white blood count was higher. Each group also showed small differences by the presence of associated features, such as pleural effusion, otitis media, tonsillitis, and anaemia.

TABLE I.—*Comparison of Main Features of Stoss and Standard Groups*

		Stoss	Standard
Total in group		52	54
Age	1/12–1 year	11	14
	1–2 years	9	12
	2–4 ,,	14	12
	4–6 ,,	11	11
	6–12 ,,	7	5
Sex:	Boys	30	31
	Girls	22	23
No. severely ill		14	12
Average No. of days ill before admission		3·5	5
Previous history of acute lower respiratory infection		18	11
Immediate previous chemotherapy		4	14
Mean temperature on admission	Oral	103° F. (39·4° C.)	102·1° F. (38·9° C.)
	Rectal	101·7° F. (38·7° C.)	102·7° F. (39·3° C.)
Mean pulse rate on admission		136	132
Mean respiratory rate on admission		39	45
Radiological grouping	Group 1a	22	22
	,, 1b	2	5
	,, 2a	7	3
	,, 2b	4	4
	,, Mixed 2a and 2b	0	1
	,, 3	17	19
White blood count (cells c.mm.). No. of patients		51	46
Over 20,000		7	3
15,000–20,000		12	8
10,000–15,000		14	13
Under 10,000		18	22
Additional features on admission	Pleural effusion	3	1
	Otitis media	0	4
	Tonsillitis	1	0
	Anaemia	2 (Hb 8·9 g.% and 7·5 g.%)	1 (Hb 8·6 g.%)

Treatment.—Of 52 stosstherapy children, 48 received both sulphadimidine and penicillin; 4 had penicillin alone. The sulphadimidine was given by mouth. The dose was 0.3 g. per kg. up to a usual maximum of 4 g.; one robust child was given 5 g. The penicillin was given by intramuscular injection. 39 children were given, in addition to sulphadimidine, 0.2 to 0.5 mega unit of sodium penicillin; nine had, in addition to sulphadimidine, 0.3 mega unit of procaine penicillin with 0.1 mega unit of sodium penicillin (= 1 ml. "seclopen"). Three children had only 1 ml. of seclopen; one had only 0.3 mega unit of sodium penicillin. In the standard group, treatment was either with repeated intramuscular injections of

penicillin or by such penicillin treatment combined with sulphadimidine. Penicillin injections were given six-hourly when the sodium salt was used and once or twice daily when seclopen was used. The dose of sulphadimidine was 0.15 to 0.2 g. per kg. per 24 hours, and this was given six-hourly in divided doses by mouth. Treatment was continued for at least five days.

Results of Treatment

Treatment was considered successful if the initial response was satisfactory and improvement maintained, if treatment did not need to be repeated or changed, and if there were no relapses or complications. Failures were those who did not respond to the initial treatment and who required a change of treatment. Relapses were those who deteriorated after an initial apparently satisfactory response. There was one patient who responded incompletely; this child improved initially, but improvement was not maintained. Table II shows the overall results of treatment.

TABLE II.—*Summary of Response to Treatment*

	No.	Successes	Failures	Relapses	Complications	Incomplete Response
Stoss ..	52	43	2	3	3	1
Standard	54	46	4	0	4	0

Failures.—Of the two failures in the stoss group one was subsequently given a course of penicillin and sulphadimidine, failed to respond, and was finally given a course of chlortetracycline with fair results: the other was subsequently given a course of penicillin and sulphadimidine, and responded fairly well. Of the four failures in the standard group, one responded well when sulphadimidine was added to the penicillin already being given, two responded fairly well to the substitution of chlortetracycline, and one failed to respond to chloramphenicol with sulphadimidine but subsequently made a fair response to chlortetracycline. It may be significant that these four patients had normal radiographs.

Relapses.—Of the three relapses in the stoss group, two were given a second stoss dose and one a course of penicillin and sulphadimidine. All three responded well.

Complications.—The complications were all extrapulmonary. The three patients in the stoss group with complications (two with otitis media and one with pharyngitis) responded well to a single further injection of penicillin and the four in the standard group (two with otitis media and two with pharyngitis) to a further course of penicillin.

Further Study of Response to Treatment

This response is considered under the headings of temperature, pulse, respiration, signs in the chest, radiological signs, and length of stay in hospital. The analyses have been confined to the 43 patients in the stoss group and the 46 in the standard group who were classified as successes (Table II).

Temperature

In children under 5 years of age all readings (except in one child in whom readings were axillary) were taken rectally; in children 5 years or over it was taken by mouth. Readings were made every four hours. The exclusions were:

	Stoss	Standard
Exclusions:		
Afebrile on admission	3	6
Delayed treatment	1	0
Axillary readings	0	1
No. analysed	39	39

"Afebrile" includes any patient whose rectal temperature was under 100.2° F. (37.9° C.) or whose oral temperature was under 99.2° F. (37.3° C.). The number remaining for analysis was 39 in each treatment group. The temperatures were rectal readings in 31 and 26 patients in the stoss and standard groups respectively. As there is no agreement on the exact figure which represents a normal temperature, and the site at which the temperature is recorded influences the reading (Moncrieff and Hussey, 1948), evaluation of response has been based on fulfilment of two criteria:

Criterion I.—The duration of time in hours from the temperature recording just preceding the beginning of treatment to the time when the temperature first touches 100° F. (37.8° C.) or lower in the rectal series, and 99° F. (37.2° C.) or lower in the oral series.

Criterion II.—As for Criterion I, but the temperature must remain at 100° F. (37.8° C.) rectally or lower for a period of at least 24 hours, and 99° F. (37.2° C.) or lower for the oral series.

The fulfilment of criteria I and II for the rectal readings is illustrated in Figs. 1 and 2. It can be seen that there were considerably more which fulfilled criteria I and II

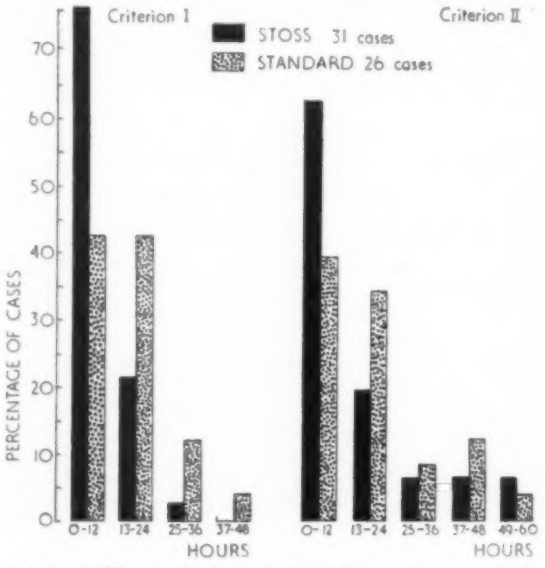

FIG. 1.—Fulfilment of criteria I and II for temperature (rectal).

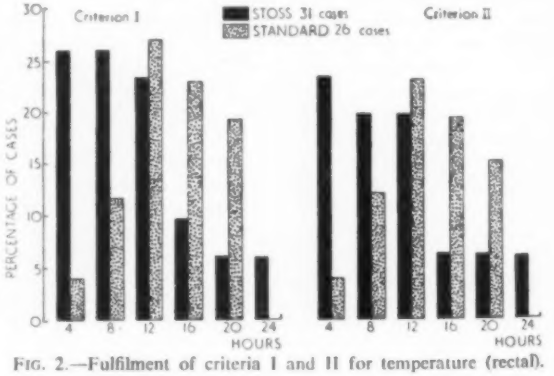

FIG. 2.—Fulfilment of criteria I and II for temperature (rectal).

earlier in the stoss group. For instance, 52% in the stoss group compared with 16% in the standard group, and 42% compared with 16%, fulfilled criteria I and II respectively within eight hours of treatment. Similar observations were made in the oral series.

In order to exclude the possible relationship of the height of the temperature on admission to the speed with which it responded to treatment, the stoss and standard groups of patients were subdivided into two groups according to whether their temperature on admission was 102.4° F. (39.1° C.) and under, or 102.6° F. (39.2° C.) and over. These two groups were analysed with reference to the speed with which criterion II was fulfilled. For the lower-temperature group, stoss was more efficient than standard in fulfilling criterion II; thus more than 50% of the 23 patients in the

stoss group fulfilled criterion II within eight hours of treatment, compared with 8% of the 13 patients in the standard group. For the higher admission temperature, stoss and standard treatments were about equally effective.

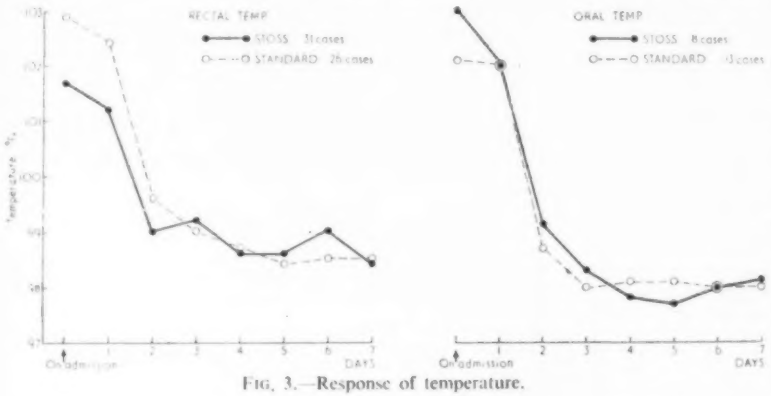

FIG. 3.—Response of temperature.

Temperature Chart for the First Seven Days.—The mean temperature recording for each day was calculated (Fig. 3). The first figure was the first reading taken on admission in the ward. The second figure, day 1, was the mean of the readings taken on the day of admission. On each full day the temperature shown in Fig. 3 was the mean of five readings for each child. For instance, the figure for day 2 was the mean of 285 readings by the rectal route for both treatment groups. It can be seen that the curves in the rectal and oral series were very similar.

Pulse Rate

The exclusions from the analysis of the pulse rate were:

	Stoss	Standard
Exclusions:		
Delayed treatment	1	0
Notes mislaid	1	0
No. analysed	41	46

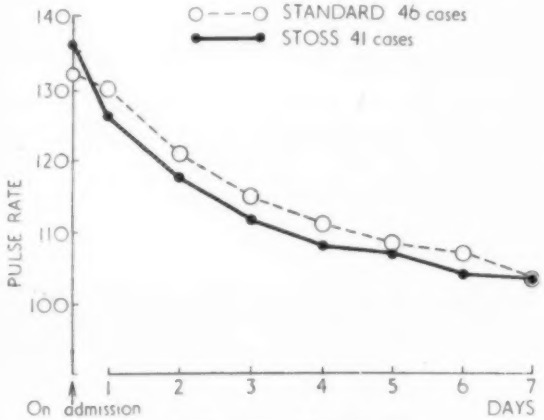

FIG. 4.—Response of the pulse rate.

The mean pulse rate on admission was 136 in the stoss group and 132 in the standard group. There were a greater number of stoss cases with very high pulse rates—for example, 7% of the patients analysed in the stoss group had pulse rates over 160 a minute, compared with none in the standard group.

Fig. 4 shows the curve for each treatment group; the response was very similar, but there was a sharper initial drop in the stoss group in spite of a slightly higher rate on admission.

Respiratory Rate

The exclusions from the analysis of the respiratory rate were the same as for the pulse rate. The mean respiratory rate on admission was 39 in the stoss group and 45 in the standard group. Although the mean rate was higher in the standard group, there were a greater number of patients in the stoss group who on admission had a very high respiratory rate (76 to 85 per minute). Fig. 5 shows the course of the respiratory rate over the first seven days. The two curves were very similar.

Rise of Temperature, Pulse Rate, and Respiratory Rate After Admission

The temperatures and pulse and respiratory rates of many of the children rose after admission, although treatment had already been started. The initial ward readings, taken on admission, were therefore compared with the highest readings above these values in the first 24 hours. The average rise in the stoss and standard groups was thus calculated. Table III and Fig. 6 show the incidence and extent of this rise of temperature and of pulse and respiratory rates which occurred within the first 24 hours of admission. The difference in the numbers analysed for temperature can be accounted for by the inclusion of three and six patients in the stoss and standard groups respectively who were afebrile on admission, and the exclusion of one patient in the stoss group whose records were mislaid.

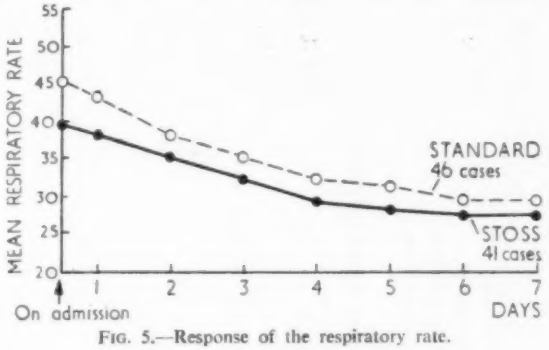

FIG. 5.—Response of the respiratory rate.

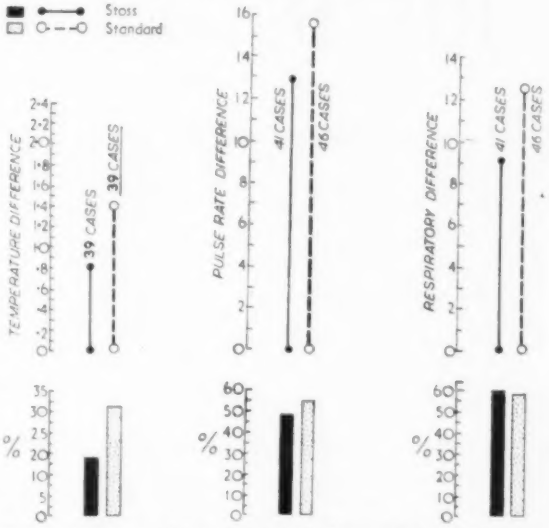

FIG. 6.—The lower figure shows the incidence of rise of temperature, pulse, and respiration above that on admission within 24 hours following treatment. The upper figure shows the magnitude of this rise.

TABLE III.—*Incidence of Magnitude of Rise of Temperature, Pulse and Respiratory Rates Within 24 Hours Following Treatment*

	Temperature	Pulse	Respiration
Incidence			
Stoss	7 (17½%)	20 (49%)	25 (61%)
Standard	14 (31%)	25 (54%)	27 (58%)
Magnitude			
Stoss	0·8° F.	13	9
Standard	1·4° F.	16	13

The greatest difference between the two treatment groups was in respect of the temperature rise. A rise of temperature after admission occurred nearly twice as often in the standard group as in the stoss group, and this rise was also nearly twice as great. The differences for rise in pulse and respiratory rates were smaller, but nevertheless showed the same trend except that the incidence of a rise in respiratory rate was the same in both groups.

Physical Signs in Chest

Physical signs in the chest were recorded on alternate days or more frequently. The rate of disappearance of signs in the chest was analysed.

Fig. 7 shows the day on which signs in the chest cleared. The mean time for each group to clear was 6.3 and 8.3 days for stoss and standard respectively. By the end of one week 28 (72%) of the stoss group compared with 20 (46%) of the standard group, and by the tenth day 37 (95%) compared with 31 (71%) respectively, had clear chests. The number of days before 50% of patients were free of chest signs was 5¼ in the stoss and 8¼ in the standard groups.

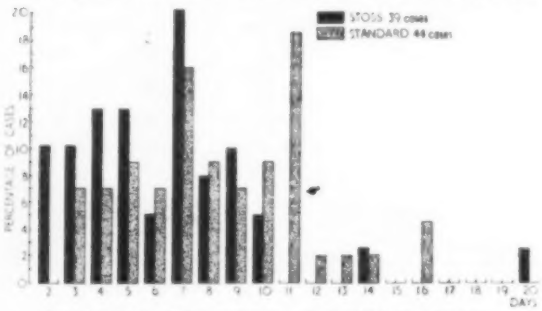

FIG. 7.—Rate of disappearance of physical signs in chest.

Clearing of Radiographs

The average time at which the chest film had returned to normal was difficult to assess because some patients failed to attend for follow-up at the appointed time; in some of these a radiograph was finally taken some weeks later, and therefore the earliest time for the chest radiograph to have returned to normal may have been missed.

After exclusion of those who had radiographs taken at more than fortnightly intervals, and of those whose radiographs were normal on admission, there remained 12 in the stoss group and 13 in the standard group. Table IV shows the results, which did not reveal any substantial difference between the two treatment groups.

TABLE IV.—*Average Time of Return of Radiograph to Normal*

	No.	Weeks						
		1	2	3	4	5	6	Over 6
Stoss	12	3	4	4	0	1	0	0
Standard	13	2	5	4	1	1	0	0

Length of Stay in Hospital

The length of stay in hospital has been analysed, although it was realized that there were many variable factors which influenced it, such as home conditions and the individual preference of the physician. In the stoss group 42, and in the standard group 46, patients remained for analysis after exclusion of one in the stoss group in whom treatment had been delayed. Fig. 8 shows the percentage of patients who were discharged each day. By the 10th day 21 patients (50%) in the stoss group and 14 (30%) in the standard group had been discharged from hospital. The mean day of discharge was 12.3 in the stoss group and 13.1 in the standard group.

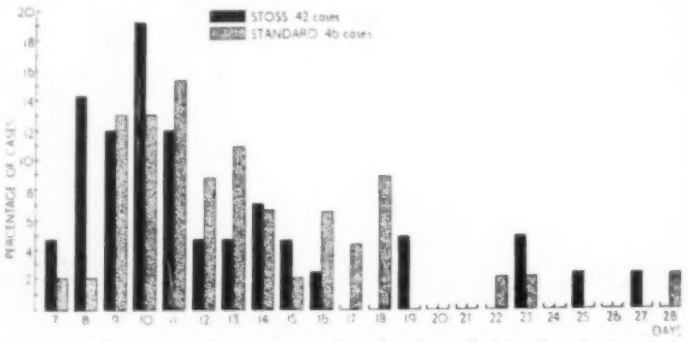

FIG. 8.—Length of stay. Percentage of patients discharged each day.

Secondary Fever

A secondary rise of temperature occurring between three and seven days after starting treatment was observed in many patients of both groups. In the present series it has been recorded if the rectal temperature rose to 100.2° F. (37.9° C.) and over, or the oral to 99.2° F. (37.3° C.) and over within seven days of admission, provided the temperature had been below these levels for 24 hours or more. The incidence and the highest readings in patients who had secondary fever are shown in Table V.

This secondary rise of fever occurred in 10 children (23 readings) in the stoss group of 41 patients and in 8 children

TABLE V.—*Maximum Readings (°F.) in Patients with Secondary Fever*

	Total	No.	99·2–100	100·2–101	101·2–102	102·2–103
Stoss	33 (rectal)	7	0	4	2	1
	8 (oral)	3	3	0	0	0
Standard	32 (rectal)	4	0	4	0	0
	13 (oral)	4	3	1	0	0

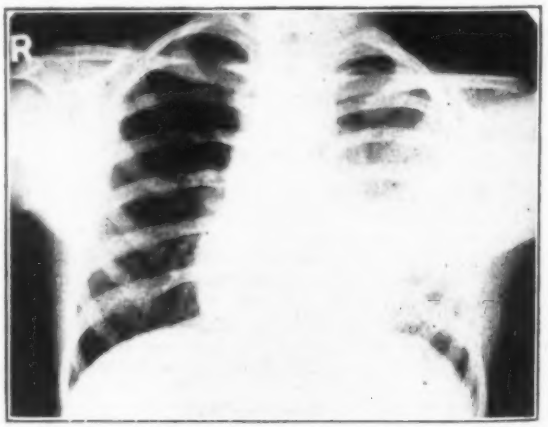

FIG. 9.—Case 61 on admission. Left upper lobe consolidation.

(12 readings) in the standard group of 45 patients. The most common day on which secondary fever occurred was the fifth (in four patients) following stosstherapy, and the sixth (in four patients) following standard therapy. Secondary fever after stosstherapy has been recognized by previous observers (Platt, 1940; Minetto, 1944; Lauria, 1947; Wilken-Jensen, 1948), but no satisfactory explanation for its occurrence has been offered. In Platt's series, 14 of his 41 patients developed a secondary rise of fever on day 2 or 3, and two others on day 6. It was surprising to find that this rise occurred in as many as 18% following standard therapy. It is important to know that this secondary rise of fever occurs in about one in three or four patients following stosstherapy, for by itself it is not an indication for further treatment.

Illustrative Cases

Typical Response. Case 61.—A girl aged 7½ years was admitted to hospital twelve hours after the onset of vomiting and pain in the left side of her chest. She was ill, and had

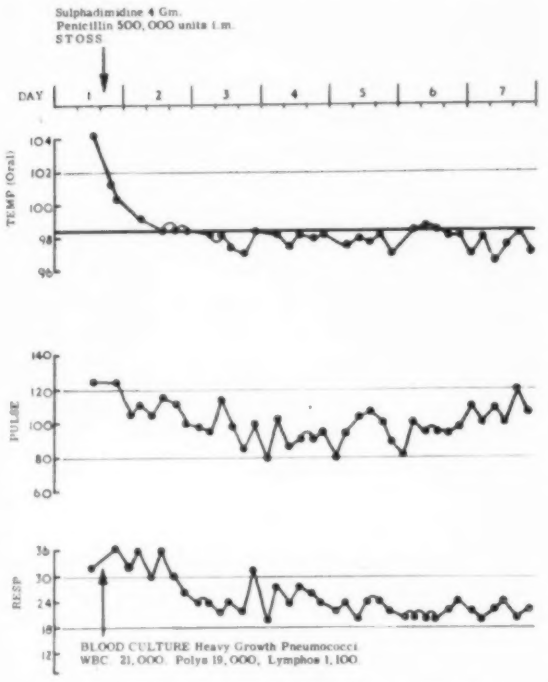

FIG. 10.—Progress of Case 61 treated by stosstherapy.

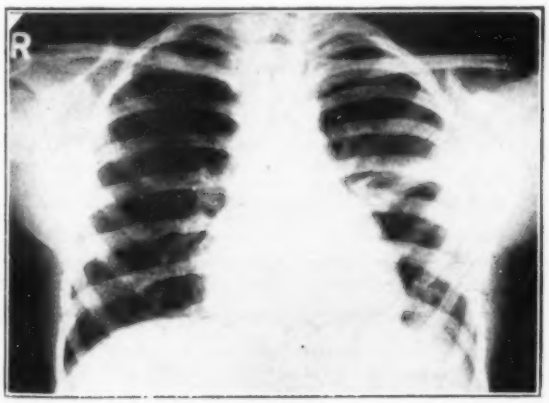

FIG. 11.—Case 61, 13 days after treatment: pleural thickening oblique fissure.

signs of consolidation over the left upper zone (Fig. 9); neck stiffness and Kernig's sign were also present. She was treated with sulphadimidine, 4 g. by mouth, and 500,000 units of sodium penicillin by intramuscular injection. Her subsequent clinical and radiological progress is shown in Figs. 10 and 11. On the next day she was better in all respects. She continued to make good progress; by the seventh day no signs were present in the chest, and she was getting up. By the thirteenth day her chest was almost normal radiologically (Fig. 11). She was discharged home on the fourteenth day, having gained 3 lb. (1.4 kg.) in weight.

Relapse. Case 48.—An ill boy aged 5¼ years was admitted to hospital with a right lower lobe pneumonia (Figs. 12 and 13). He responded well to stosstherapy, but on the ninth day relapse occurred and he was given a second stoss dose of 3.5 g. of sulphadimidine and 500,000 units of sodium penicillin, to which he responded well. Secondary fever occurred three days after this second dose (shown as 12th day in Fig. 12).

Discussion

In the treatment of acute respiratory infections with sulphonamide and penicillin little attention has been given to consideration of the minimum duration of chemotherapy necessary. The concept that a certain blood level of sulphonamide or penicillin should be maintained for several days has dominated both dosage and the duration of treatment. A specified number of days of treatment (Medical Research Council, 1943), a specified total amount of drug, or a certain duration after the patient has become apyrexial have been some of the recommendations made. Hawking and Lawrence (1950) advised continuing the drug until the time the crisis would have occurred. As early as 1938, however, Whitby (1938), in referring to the sulphonamides, said, "Dosage and the duration of the course provide ample opportunity for the art of medicine where experience and judgment will give the best results. Experimentally and clinically it is clear that what these drugs are going to accomplish they do quickly; there is no justification for giving a prolonged course."

In reviewing the dosage of penicillin in bacterial infections, Marshall (1948) pointed out that, although it is established with certainty that the administration of adequate amounts of penicillin by a dosage schedule which maintains a more or less constant concentration of drug in the blood for a certain time will cure many severe infections, it is by no means established that this dosage schedule is the most satisfactory or the only one which is effective. He goes on to say that dosage has been based on two unproved assumptions: firstly, that it is necessary to maintain constant blood levels; and, secondly, that observations *in vitro* can be transposed without modification to human disease. Some writers, discarding the theory of constant blood levels, have recommended intermittent treatment (Bigger, 1944a, 1944b; Tumulty and Zubrod, 1948; Price *et al.*, 1949; Hamburger *et al.*, 1949). In the present series, constant blood levels were unnecessary, for results as good as those on standard treatment were obtained with stosstherapy; indeed, stosstherapy is the exact antithesis of the theory of constant blood levels. It is necessary to emphasize that, although a single dose will be sufficient in most patients, stosstherapy does not necessarily confine itself to a single dose, for an essential feature of stosstherapy is that treatment is kept under review and is guided by clinical considerations. The patient's response is reviewed at intervals of 12 to 18 hours during the first 36 hours, so that if the response has been inadequate a second stoss dose can be given or chemotherapy changed.

The results of the present investigation have shown that in acute respiratory infection in children stosstherapy produced as good results as standard treatment. A slightly but not significantly higher relapse rate occurred, but response to further stoss or standard therapy was excellent. When a more detailed analysis of the response to treatment was

made, stosstherapy was again as good as standard. In most instances the figures in the stoss group, especially those of temperature response, were better than those in the standard group. A rise of temperature, pulse rate, and respiratory rate within 24 hours after the start of treatment commonly occurred in both treatment groups, but the incidence and magnitude of the temperature rise was much less than in the stoss group.

Advantages of Stosstherapy

Many of the side-effects of the sulphonamides, such as nausea, anorexia, drug fever, leucopenia, rashes, mental changes, and haematuria, are related to the total amount of drug taken and the duration of treatment; these side-effects, therefore, are rarely seen in stosstherapy. In the present series no such effects were seen and there were no cases of macroscopic haematuria; microscopical examination of the urine was not done routinely following stoss-therapy, but no excess red cells were present in the urine of the few patients so examined. Penicillin also has side-effects, and some of the reactions are related to the duration of treatment (Lawrence *et al.*, 1953). A single injection is therefore less likely to cause these side-effects than multiple injections.

One injection compared with twenty or more is a big advantage, especially in children: pain and the fear of the next "prick" do not occur. As only a few patients need further treatment, overtreatment of many patients is avoided. Patients have less need to be admitted to hospital. All the hazards associated with injections are reduced to a minimum. From the nurses' point of view more time is available for nursing.

Repeated doses or, worse, injections disturb the patient's rest and sleep; this is particularly objectionable in ill patients during the first few days, when adequate sleep and rest are so essential. Although the newer sulphonamides cause less anorexia and nausea, some patients still experience these unpleasant side-effects. With one dose, however, nausea and anorexia do not persist for long, and the patient is able to enjoy his food sooner.

The time and labour saved by avoiding repeated doses and injections are considerable. Much time and labour are also saved in the preparation and sterilization of needles and syringes. Fewer syringes are broken. The actual expense of the drugs is also less. In 1953, when this investigation was done, stosstherapy for 50 patients cost about £3 10s. compared with £18 10s. for standard treatment; if stoss-therapy were used for all cases the saving would amount to a considerable sum in view of the frequency of respiratory infection.

A more rapid response of the temperature was observed in the stoss group; this has been observed by others (Jersild *et al.*, 1956). Stosstherapy gives an earlier indication of whether the patient is failing to respond to treatment, and a quicker change can be made to different chemotherapy.

A possible objection to stosstherapy is that a large dose of sulphonamide might cause obstruction in the urinary tract. This did not occur in over 1,500 patients treated by

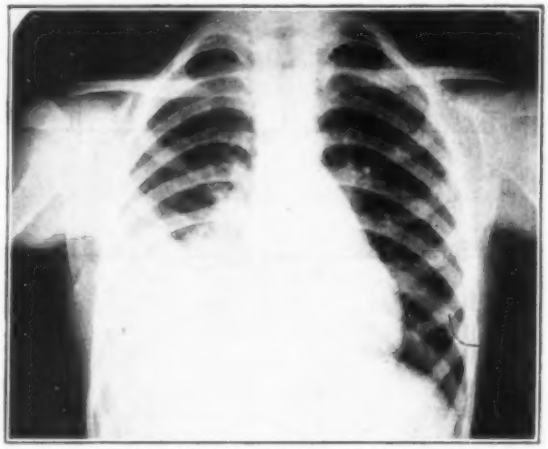

FIG. 13.—Case 48. Right lower lobe consolidation with effusion.

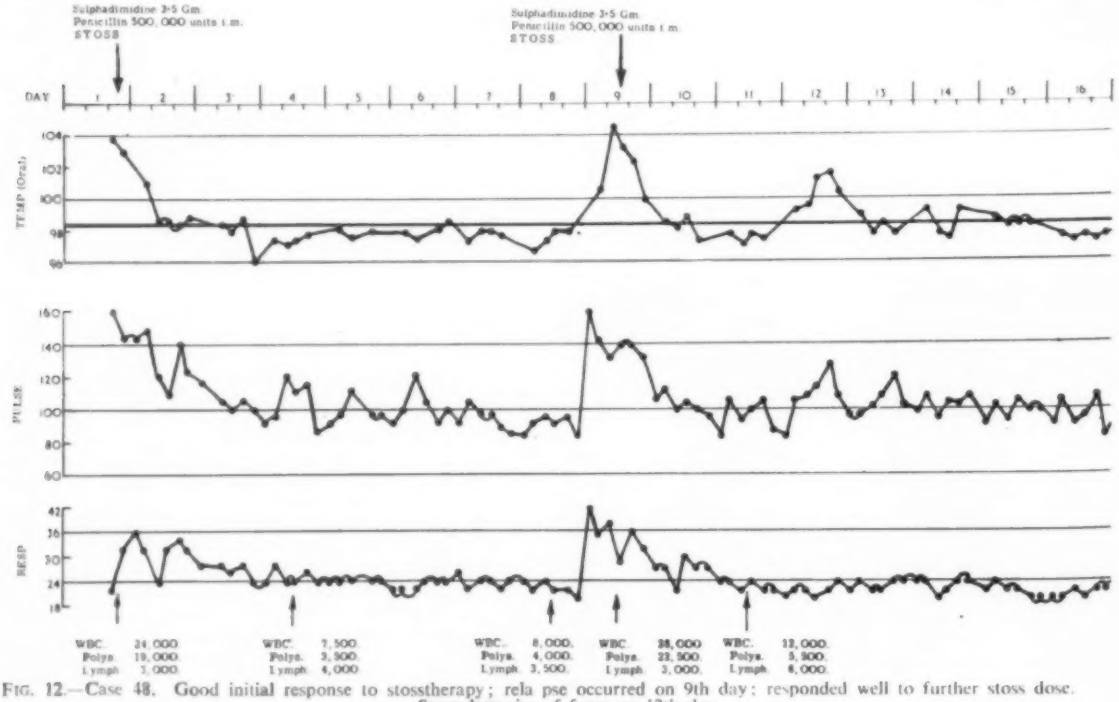

FIG. 12.—Case 48. Good initial response to stosstherapy; relapse occurred on 9th day; responded well to further stoss dose. Secondary rise of fever on 12th day.

stosstherapy so far reported. With the newer more soluble sulphonamides such as sulphadimidine, this danger is a remote one.

The general management of patients treated by stosstherapy is no different from that of patients treated by standard methods; but with stosstherapy the patient and his disease are treated rather than the disease alone. Friderichsen and Walther (1950) have pointed out that clinicians do not feel tempted to give up a certain form of treatment while good results have been so obtained. I hope, however, by having illustrated the advantages of this successful method of chemotherapy, that more will use it. I am sure that those who do so will find the change justified.

Summary

Fifty-two children with acute lower respiratory infection were treated with stosstherapy, a single massive combined dose of sodium penicillin by injection and sulphadimidine by mouth or with penicillin alone, and their response was compared with that of 54 similarly affected children treated by repeated chemotherapy given for five days or more.

The analysis of the cases was based on the overall results (successes, failure, relapses, and complications); and on the response of pyrexia, pulse, and respiratory rates; rate of disappearance of physical and radiological signs; and length of stay in hospital. The analysis showed that those children treated by stosstherapy responded at least as well as those treated by repeated chemotherapy.

The appearance of fever, most commonly occurring between the third and sixth days after both stosstherapy and standard chemotherapy, is described.

It is suggested that, as equally good results are obtained with stosstherapy, its many advantages imply that it should be the method of choice for acute infections of the lower respiratory tract in children.

I thank Dr. B. Buckley Sharp, Dr. P. R. Evans, and Dr. C. T. Potter for allowing me to use stosstherapy in the treatment of their patients. I am indebted to Professor W. Gaisford, from whom I learnt the method of stosstherapy. I thank Dr. P. R. Evans and Dr. R. C. Mac Keith for their helpful criticism, and Dr. J. Dow for his guidance in the interpretation of the radiographs. I also thank Sister T. Swindells and the nursing staff for their care and enthusiasm for this treatment. I am grateful to the medical illustration and photographic departments for the preparation of the charts and radiographs.

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MEASUREMENT OF RED-CELL LOSS FROM GASTRO-INTESTINAL TRACT, USING RADIOACTIVE CHROMIUM

BY

N. C. HUGHES JONES, B.M., Ph.D.

From the Medical Research Council's Blood Transfusion Research Unit, Postgraduate Medical School of London, W.12

When ^{51}Cr-labelled red cells are introduced into the stomach or duodenum, more than 90% of the chromium can be recovered in the faeces (Owen *et al.*, 1954; Roche *et al.*, 1957). This is not altogether surprising, since chromic oxide is virtually unabsorbed by the gastro-intestinal tract, and has been used as an index material in digestion studies in animals and in man (Hamilton *et al.*, 1928; Kreula, 1947). Roche *et al.* (1957) used the technique of injecting ^{51}Cr-labelled red cells intravenously and then estimating ^{51}Cr loss in the stools to determine the extent of red-cell loss into the gastro-intestinal tract in hookworm disease.

In the present investigation six anaemic patients who were known to be losing red cells in their stools were studied. After the intravenous injection of ^{51}Cr-labelled red cells, the loss of ^{51}Cr in the stools was estimated, and these estimates were used to correct the ^{51}Cr-survival curves. It was thus possible to discover whether or not the blood loss in the stools accounted for the diminished survival of red cells in the circulation.

Methods

Labelling of Red Cells with ^{51}Cr.—Red cells were labelled with approximately 100 μC of ^{51}Cr by the method of Mollison and Veall (1955), using ^{51}Cr with a specific activity of 10–30 μC per μg. of chromium.

Estimation of ^{51}Cr Content of Stools.—Two methods were used. *Method 1:* Daily collections of stools were made in tins (diameter, 12.5 cm.; length, 16.5 cm.), except in patient G. B., from whom collections every three to four days were made. The radioactivity in each tin was measured in a ring counter containing 32 Geiger–Müller tubes, as described by Booth and Mollin (1956). A known aliquot of the injected dose of ^{51}Cr was mixed with 100 g. of sugar and estimated at the same time, as a standard. *Method 2:* Water was added to the faeces, which were then weighed and homogenized. The radioactive content of a 10-ml. aliquot was estimated in a pillar-type scintillation counter. As a standard a similar volume of a 1 in 100 dilution of the injection suspension of red cells was used. The ^{51}Cr content of the stools on any day was expressed as a percentage of the injected ^{51}Cr.

Accuracy of Method 1.—The Geiger–Müller ring counter had a background count of 220 c.p.m., and 1 μC present in the tin gave approximately 130 c.p.m. Thus, with 20 minutes' counting of the background alone and 20 minutes with the source, 1 μC of ^{51}Cr could be estimated with a coefficient of variation of 4%. If 100 μC of ^{51}Cr was injected, and the subject's red-cell volume was 2 litres, then this quantity of ^{51}Cr would represent 20 ml. of red cells. The presence of 0.1 μC of ^{51}Cr, representing 2 ml. of cells, could just be detected if the background counts alone and the background counts together with the ^{51}Cr source were each counted for one hour.

Accuracy of Method 2.—A concentration of 1 μC in 100 ml. gave 1,200 c.p.m. in the scintillation counter and the background counts were of the order of 40 c.p.m. 2,500 counts were usually made, and the coefficient of variation was 2%. A concentration of 0.004 μC per 100 ml. could

just be detected, representing 0.04 ml. of red cells per 100 ml. of homogenized stool, at the beginning of the experiment.

Red-cell Survival Estimates

Blood was collected 10 minutes after injection, and this value was taken to represent 100% survival. Blood samples were withdrawn at suitable intervals thereafter. Corrections for changes in the packed cell volume were made during the first three days only; thereafter it was assumed that the blood volume remained constant. The figures published by Mollison and Veall (1955) were taken to represent the normal survival curve.

Correction of the Observed ^{51}Cr.-survival Curve for the Loss of ^{51}Cr in the Stool

The percentage of the blood volume lost in the stool on any day, t, was obtained, using the following formula:

$$L = S \times \frac{100}{B}$$

where L = percentage of the blood volume lost in the stool on day t

S = percentage of the injected ^{51}Cr in the stool on day t

B = ^{51}Cr survival in the blood on day t (expressed as a percentage).

This calculation was made for each day on which stools were obtained. The ^{51}Cr survival in the blood was obtained by interpolation from the graph of the ^{51}Cr-survival curve, and the value used was that for the middle of the stool collection period.

When ^{51}Cr-labelled red cells are lost in the stools, then the subsequent ^{51}Cr concentration in the blood of the remaining cells will be diminished in proportion to the percentage of labelled cells left in the circulation—that is, by "the percentage of the blood volume not lost in the stools." Thus the correction of the survival curve for the ^{51}Cr loss in the stools was carried out by multiplying the observed ^{51}Cr-survival estimate on any day, t, by the values

$$\frac{100}{\text{percentage blood volume not lost in the stools}}$$

for each of the preceding days—that is:

$$B \times \frac{100}{100-L_1} \times \frac{100}{100-L_2} \times \frac{100}{100-L_{(t-1)}}$$

where B = the observed ^{51}Cr-survival value on day t

$L_1, L_2, L_{(t-1)}$ = percentage of the blood volume lost in the stools on day 1, 2, etc.

Calculation of Red-cell Loss in Stools

The following formula was used for this calculation:

$$\text{Red-cell loss (ml.)} = \frac{P}{C} \times B.V. \times \frac{PCV \times 0.91}{100}$$

where P = ^{51}Cr in the stool, as a percentage of the dose injected as labelled cells

C = percentage ^{51}Cr survival in the blood on that day

PCV = packed cell volume, as a percentage of venous blood, after correction for trapped plasma. The factor 0.91 is introduced into the formula to take into account the "body haematocrit/venous haematocrit" ratio (Chaplin *et al.*, 1953).

BV = total blood volume (ml.). This was obtained from the ^{51}Cr data. For the purpose of the calculations it was assumed that the total blood volume remained constant through the observations.

Occult Blood Test on Stools.—The modified Gregerson test, described by Needham and Simpson (1952) was used.

Results

Absorption of ^{51}Cr by the Gastro-intestinal Tract

^{51}Cr-labelled cells were introduced into the stomachs of two patients who were undergoing milk-drip therapy for peptic ulcers. One patient (A) was given 1.4 ml. of cells labelled with 21 μC of ^{51}Cr (1.5 μg. of chromium), and the other patient (B) was given 2.5 ml. of cells labelled with 8 μC of ^{51}Cr (0.6 μg. of chromium). The stools were then collected daily until their ^{51}Cr content had fallen to zero. The ^{51}Cr content was estimated by both methods (see above), and the results were found to agree closely (see Table I). Patient A excreted 66% and patient B 87% of the administered ^{51}Cr.

TABLE I.—*Percentage Recovery of ^{51}Cr in Stools (Estimated by Two Methods) Following Introduction of ^{51}Cr-labelled Red Cells Into the Stomach*

		Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Total
Patient A	Method 1	46·4	20·2	0				66·6
	,, 2	47·2	17·6	0				64·8
,, B	,, 1	17·6	33·4	31·6	2·2	1·9	0	86·7
	,, 2	17·0	36·6	31·0	—	—	—	

^{51}Cr Excretion in Patients not Losing Blood in the Stools

Investigation was made of two patients who were thought not to be losing red cells in the stools. One (A. S.) was a 34-year-old man undergoing radiotherapy for seminoma of the testis, the other (M. H.) was a 57-year-old woman with a normochromic anaemia of unknown aetiology. During the course of the investigations all occult blood tests on the stools were negative. Six collections of stool were made from each patient; the percentage of the injected dose of ^{51}Cr excreted each day, together with the red-cell equivalent, is given in Table II. In A. S. not more than a ten-thousandth part appeared in the stool each day, and in M. H. not more than a two-thousandth part. If this amount of ^{51}Cr in the stool were due to the presence of red cells it would represent approximately 0.1 and 0.2 ml. of red cells lost per day respectively.

TABLE II.—*^{51}Cr Excreted Daily in the Stool in Two Patients Without Gastro-intestinal Bleeding, After Injection of ^{51}Cr-labelled Cells*

Day	Patient M. H.		Patient A. S.	
	^{51}Cr Content of Stool as Percentage of Injected Dose	Red Cell Equivalent (ml.)	^{51}Cr Content of Stool as Percentage of Injected Dose	Red Cell Equivalent (ml.)
1	0·008	0·09	0·004	0·09
2	0·015	0·17	0	0
3	0·013	0·15	0·003	0·07
4	0·019	0·24	0·007	0·16
5	0·005	0·07	0·004	0·1
6	0·014	0·19	0·008	0·2

The chemical tests for occult blood in the stools were negative throughou...

^{51}Cr Excretion in Patients Losing Blood in the Stools

Patient G. B.—Woman aged 50. Diagnosis: cavernous haemangioma of the small gut. For eight years she was persistently anaemic and had required over 100 transfusions. She had never had a melaena stool, but examinations for occult blood were almost always positive. Apart from iron-deficiency anaemia, no haematological abnormalities were found. The stools were of a slate-grey colour probably due to oral iron therapy. *^{51}Cr investigations:*—Her own red cells were labelled with ^{51}Cr and injected. On the third day after the injection she gave clinical evidence of the rapid loss of blood, and the haemoglobin concentration was found to have fallen from 8.6 to 5.4 g./100 ml. The stools were collected for 17 days, and the amount of red cells in the faeces, together with the observed and corrected ^{51}Cr concentration curves in the blood, are given in Fig. 1. On the 17th day the corrected ^{51}Cr curve was only 6% below the normal value. During this period the patient lost red cells equivalent to 79% of her red-cell mass (as estimated at the onset of the investigations). Despite this, the stools did not alter from their slate-grey colour. Later 70 cm. of jejunum was removed at operation. One small cavernous haemangioma was found.

Patient E. B.—Man aged 45. Diagnosis: aplastic anaemia. He had anaemia, leucopenia, and thrombocyto-

penia, and was originally diagnosed as suffering from thrombocytopenic purpura. However, there was no improvement after splenectomy, and in the following 18 weeks he required 81 pints (46 litres) of blood. The occult blood test on the stools was persistently positive, but it was not certain whether the loss of blood by this route was sufficient to account for the anaemia or whether a

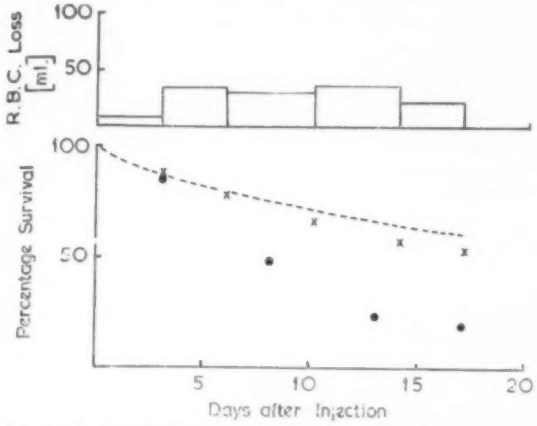

FIG. 1.—Patient G. B. Cavernous haemangioma of small gut. The observed and corrected ^{51}Cr concentrations in the blood are shown, together with the red cell loss in the stools, after the injection of ^{51}Cr-labelled red cells. ●=Observed ^{51}Cr concentration in the blood. ×=^{51}Cr concentration in the blood, corrected for red-cell loss in the stools (for method of calculation, see text). - - - -=normal ^{51}Cr survival curve (from Mollison and Veall, 1955).

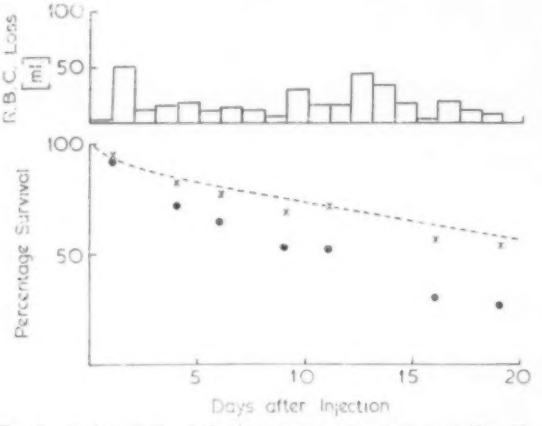

FIG. 2.—Patient E. B. Aplastic anaemia. (Symbols as in Fig. 1.)

haemolytic process was also present. *^{51}Cr investigations*:—Compatible red cells from a donor were labelled with ^{51}Cr and injected. The stools were collected for the following 19 days; the amount of red cells in the faeces and the observed and corrected ^{51}Cr concentrations in the blood are given in Fig. 2. During this period the patient lost 400 ml. of red cells in the stools, which were dark brown in colour throughout. On the 19th day the corrected ^{51}Cr concentration in the blood was only 5% below the normal value.

Patient G. G.—Man aged 37. Diagnosis: ulcerative colitis. He was investigated during a relapse of his disease. Blood was not usually visible macroscopically in his stool, but the occult blood tests were positive. The haemoglobin concentration varied between 9.5 and 12.5 g./100 ml. and the reticulocyte count was between 1 and 4%. *^{51}Cr investigations*:—His red cells were labelled with ^{51}Cr and injected. The stools were collected for the next 24 days. The faecal loss of red cells and the observed and corrected ^{51}Cr concentrations in the blood are shown in Fig. 3. The corrected ^{51}Cr value on day 24 was 50%—that is to say, 2% below the normal value.

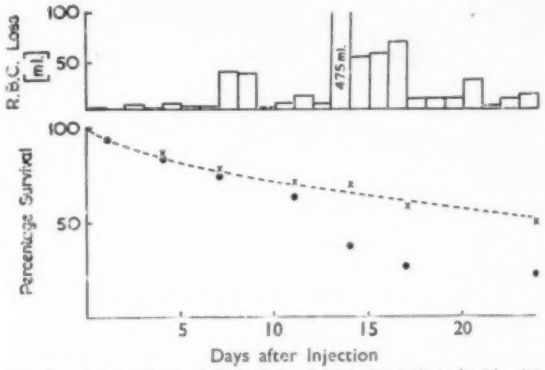

FIG. 3.—Patient G. G. Ulcerative colitis. (Symbols as in Fig. 1.)

Patient V. P.—Woman aged 57. Diagnosis: hereditary haemorrhagic telangiectasia. She had been intermittently anaemic since the age of 18. When seen she had an iron-deficiency anaemia with a haemoglobin concentration of 7 g./100 ml. The occult blood test in the stool was persistently positive. *^{51}Cr investigations*:—Her red cells were labelled with ^{51}Cr and injected. During the following seven days 10% of the injected ^{51}Cr was lost in the stools. The corrected ^{51}Cr concentration in the blood on the seventh day was 77% (normal value, 78%).

Patient J. H.—Girl aged 18. Diagnosis: Fanconi type of refractory anaemia. She had received several hundred pints of blood during her lifetime; she was losing blood through the nose, mouth, rectum, and vagina, but it was not certain whether this loss, together with the aplastic marrow, would account for the degree of anaemia, or whether a haemolytic process was also present. *^{51}Cr investigations*:—Compatible cells were labelled with ^{51}Cr and injected. All stools and vomit were collected over the next 21 days, together with swabs containing blood from the nose and vagina. During this period 16% of the injected dose of ^{51}Cr was lost; the corrected ^{51}Cr concentration in the blood on the 21st day was 58%, compared with the normal value of 55%.

Patient R. G.—Woman aged 61. Diagnosis: iron-deficiency anaemia. Barium enema showed multiple diverticula of the sigmoid and descending colon, and the occult blood tests were positive throughout the observation period. *^{51}Cr investigations*:—Her own cells were labelled with ^{51}Cr and injected. The stools were collected during the next 13 days; their ^{51}Cr content varied between 0.03 and 0.21% of the injected dose and the total excreted during this period was 1.1% (average daily excretion, 0.083%). This represented a total loss of 13.5 ml. of red cells, or, on the average, 1 ml. of red cells a day. The loss of ^{51}Cr in the stools of this patient was 7 and 20 times greater than that found in patients A. S. and M. H., who were thought not to have lost red cells in their stools. The loss of ^{51}Cr in the stools was too small to affect the ^{51}Cr survival curve.

Discussion

Neither Owen *et al.* (1954) nor Roche *et al.* (1957) were able to recover all the ^{51}Cr in the stools after introducing ^{51}Cr-labelled red cells into the stomach or duodenum of their subjects. The estimates of recovery made on eight patients by Roche *et al.* were between 90 and 103%. Recoveries of only 65 and 88% were obtained in the present investigation. A small quantity of the ^{51}Cr introduced into the gut as ^{51}Cr-labelled red cells must therefore be absorbed. Nevertheless the amount of ^{51}Cr absorbed must be extremely small, as the quantity given was only of the order

of 1 μg. Other estimates of the absorption have been made in man, using the insoluble chromic oxide (Kreula, 1947; Irwin and Crampton, 1951). These investigators stated that it was virtually unabsorbed, but they were given 4–15 g. and hence the absorption of μg. quantities could not be detected.

In four of the five patients presented here the corrected ^{51}Cr concentration in the blood at the end of the investigation was between 1 and 6% lower than the normal ^{51}Cr value. It is reasonably certain that this discrepancy was due to reabsorption of some of the ^{51}Cr by the gut. It would be difficult to correct precisely for this absorption, because the amount absorbed probably varies with the site of bleeding—that is, there would be greater absorption after bleeding into the stomach than after bleeding into the descending colon. It remains possible that the apparent slight diminution of ^{51}Cr survival in the blood was due to a haemolytic process. However, the process would have had to be very mild. Thus, in patient G. B., in whom ^{51}Cr curves showed the greatest departure from normality, the apparent loss of red cells was only 0.25% a day, whereas in haemolytic anaemia of clinical significance the loss is from 3 to 20% a day.

Roche *et al.* (1957) found that the excretion of ^{51}Cr in the stools in 10 subjects without evidence of gastro-intestinal bleeding was equivalent to 1.27 ml. of blood a day. As their subjects had approximately normal haemoglobin concentrations, this amount of blood probably represented about 0.5 ml. of red cells. The quantities found in the two subjects studied here were less than this—namely, 0.1 and 0.2 ml. of cells a day. Roche *et al.* did not wash the red cells after labelling with ^{51}Cr, and hence approximately 10% of the injected ^{51}Cr was present in the plasma. This unattached ^{51}Cr may account for their higher normal values. Owen *et al.* (1954) found a greater amount of ^{51}Cr in the stools after the injection of sodium chromate intravenously than after the injection of ^{51}Cr-labelled red cells. In the present investigation the red cells were washed free from unabsorbed ^{51}Cr before injection.

Owen *et al.* (1954) have also shown that ^{51}Cr is excreted in the stools after the intravenous injection of trivalent ^{51}Cr (red cells are not labelled by trivalent ^{51}Cr); thus the ^{51}Cr found in the stools in normal subjects could be derived either from the ^{51}Cr which elutes out of surviving red cells or from that which is freed from cells destroyed within the body. On the other hand, there may be a small loss of red cells into the gut each day.

Both the ^{51}Cr-labelling and the occult blood tests using benzidine are unsatisfactory when only small amounts of red cells are lost in the stools. The occult blood tests using the peroxidative activity of haemoglobin are limited, because if they are made too sensitive other peroxidases present in faeces will give false-positive results. The ^{51}Cr-labelling method is limited because ^{51}Cr is normally excreted in the stools after the injection of labelled cells. Needham and Simpson (1952) recommended the use of 0.5% benzidine solution for the occult blood tests, and they found that it was necessary to give approximately 2 ml. of cells by mouth before a positive occult blood test could be obtained. The use of ^{51}Cr will enable 2% of this amount of red cells to be detected—that is, 0.04 ml. of cells (see method 2)—but this advantage will be offset by the normal excretion of ^{51}Cr, equivalent to 0.1–0.5 ml. of cells a day. Hence the ^{51}Cr method is useful only when the chromium excreted exceeds the equivalent of 0.5–1 ml. of red cells a day.

Summary

Blood loss in the stools can be estimated quantitatively by labelling a sample of the subject's red cells with radioactive chromium (^{51}Cr), reinjecting the cells into the circulation, and subsequently estimating the ^{51}Cr content of the stools. This method of investigation was used in six patients known to be bleeding from the gastro-intestinal tract. As expected, the rate of loss of ^{51}Cr from the blood stream was increased, and this was almost completely accounted for by the amount of ^{51}Cr lost in the stools. The fact that the amount of ^{51}Cr in the stools did not completely account for the rate of loss of ^{51}Cr from the blood stream indicates that some ^{51}Cr is reabsorbed from the gastro-intestinal tract (but is not reutilized). Thus the ^{51}Cr method slightly underestimates the amount of blood lost in the stools.

In two control subjects who were thought not to be bleeding into the gastro-intestinal tract, the amount of ^{51}Cr excreted in the stools following the intravenous injection of ^{51}Cr-labelled cells was very small (equivalent to 0.1 to 0.2 ml. of red cells a day). Because of this slight excretion of ^{51}Cr in the stools of normal subjects whose cells have been labelled with ^{51}Cr, the daily loss of blood in the stools must exceed 1 ml. a day before it can be detected by this method.

I am indebted to Dr. P. L. Mollison for his advice and encouragement throughout these investigations. Dr. D. L. Mollin kindly lent the Geiger-Müller ring counter. Professor J. McMichael, Drs. C. L. Cope, I. Gilliland, M. D. Milne, and S. Sherlock kindly allowed me to investigate patients under their care.

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EFFECT OF RESERPINE IN THERAPEUTIC DOSAGE ON EXCRETION OF 5-HYDROXYINDOLEACETIC ACID

BY

A. TODRICK, Ph.D., F.R.I.C.

M. DICK, B.Sc.

AND

A. C. TAIT, M.B., D.P.H., D.P.M.

Department of Clinical Research, Crichton Royal, Dumfries

Recent investigations into the biochemistry of 5-hydroxytryptamine (H.T.) have provided evidence that the endogenous H.T. in the mammalian brain is mobilized and disappears from the organ following the injection of reserpine (Brodie *et al.*, 1955); the hypothesis has been advanced that the latter drug owes its pharmacological properties, hypotensive and ataractic, to its ability to set free H.T. or, as an alternative, to interfere with the H.T.-binding sites, the immediate liberation being incidental.

Reserpine will also set H.T. free from blood platelets *in vitro* (Shore *et al.*, 1956) and *in vivo* in animals and man (Haverback *et al.*, 1956a), but the stores of this compound in the intestinal cells are not so readily liberated, although this has been reported following high dosage in the rabbit (Pletscher *et al.*, 1955). A resultant increase in the excretion product, 5-hydroxyindoleacetic acid (H.I.A.A.), has been demonstrated in the dog following massive doses of reserpine; the dose used, 5 mg./

kg., was 50–100 times the therapeutic dose (for ataraxis) in man (Shore *et al.*, 1955).

In view of the importance of reserpine in psychiatry, it appeared desirable to investigate whether these changes could be observed in man following treatment with therapeutic dosages of the drug. Failure to demonstrate such changes could be regarded as reducing the probability of the hypothesis mentioned above.

Of the possible alternatives, the excretion of H.I.A.A. was chosen on technical grounds as the first subject for study.

Haverback *et al.* (1956b) have reported no significant increase in H.I.A.A. excretion by six individuals receiving reserpine, but the conditions differed from those used in the present study. More recently there have been preliminary reports of an increase in H.I.A.A. excretion following reserpine (Fraser *et al.*, 1957 ; Valcourt, 1957).

Methods

The procedures and techniques used have been modified in the course of the investigation. Those described here were employed throughout the final series of tests, which are the only ones reported in detail.

Plan of Test.—All patients were males from an admission ward, the staff of which had previously collaborated in the preliminary studies. It was planned that cases should consist, so far as possible, of two equal groups of (*a*) schizophrenics and (*b*) neurotics and psychopaths ; the diagnosis was unknown to the laboratory until the completion of the investigation. Each patient was kept in bed for the duration of the test ; the bladder was emptied at 10 p.m. on the evening before the injection was to be given, and all urine was then collected separately over the following periods : 10 p.m.–7 a.m. ; 7–11 a.m. ; 11 a.m.–3 p.m. ; 3–7 p.m. ; 7–10 p.m. Reserpine ("serpasil"), 5 mg., was injected intramuscularly immediately following the completion of the 7–11 a.m. collection. Specimens were collected in brown glass bottles containing 1–2 ml. of concentrated hydrochloric acid (Scandrett, 1956). They were received in the laboratory within five hours of the end of the collection, brought to *p*H 3, and stored overnight in a refrigerator for analysis next morning.

Estimation of 5-Hydroxyindoleacetic Acid

After the brief initial report that H.I.A.A. could be estimated by its reaction with 1-nitroso-2-naphthol (Udenfriend *et al.*, 1955a), the possibilities of this reaction were studied : a second compound producing a colour with the reagent was detected chromatographically in some urines. Separation of this chromogen and examination of the absorption spectrum of the coloured reaction product suggested that it would not interfere if the optical density of the colour from H.I.A.A. were read at 640 mμ instead of 540 mμ.

The method of Udenfriend *et al.* (1955b) was later adopted in essence, but the modification of reading at 640 mμ was retained, the chloroform extraction being omitted. In addition, since the psychiatric cases under investigation did not include any with gross disorders of carbohydrate metabolism, the treatment with acid 2,4-dinitrophenylhydrazine solution was also omitted. This permitted the doubling of the ratio of urine to ether in the extraction which compensated for the 50% loss of sensitivity incurred by reading at 640 mμ.

However, following the observation (see below) that in concentrated urines the whole of the H.I.A.A. was not estimated, the procedure was adopted of diluting the urines more or less in proportion to their concentration by taking as aliquots of the specimens a fixed fraction (one-tenth, equal to a six-minute volume) of the hourly output. Thus, for a four-hour specimen of 600-ml. volume, 15 ml. would be taken, while for an overnight (nine-hour) specimen of 270-ml. volume 3 ml. would be taken. Before extraction these were diluted to a final volume of 20 ml. with distilled water acidified to *p*H 3.

A preliminary estimation was carried out on the overnight specimen, which was both the first available and one of the more concentrated ones ; 3-, 6-, and 9-ml. portions of urine were diluted and the H.I.A.A. was estimated. In 7 out of the 10 cases the estimate based on the 6-ml. specimen was 90% or more of that based on the 3-ml. specimen (mean 95%) ; the actual volume subsequently taken on the six-minute aliquot basis averaged 3.9 ml.

Estimations were carried out in duplicate : where the difference between duplicates exceeded 10% the estimation was repeated.

Estimation of Creatinine

Creatinine was estimated by the method of Bonsnes and Taussky (1945) as described by Varley (1954), except that the volume of urine taken was not fixed but was related to the volume of the specimen. Where duplicates estimated at different times differed by more than 4% a repeat estimation was carried out.

Experimental Results of Preliminary Investigations

The first series of tests consisted in measuring the 24-hour excretion of H.I.A.A. by patients due to start a course of reserpine therapy. This was continued from three days before the start to about a week afterwards and at intervals

TABLE I.—*Individual Excretion of H.I.A.A. and Creatinine Before and After Reserpine (5 mg. of Reserpine Injected Intramuscularly at 11 a.m. in Every Case)*

Case No.	Period	Urine Volume (ml./hr.)	Creatinine (g./hr.)	H.I.A.A. (mg./hr.)	H.I.A.A./Creatinine Ratio (mg./g.)	% Change from Pre-Reserpine Mean	Mean % Change after Reserpine*
1	10 p.m.–7 a.m.	29	0·0625	0·182	2·92	+ 3	± 0
	7–11 a.m.	46	0·0748	0·205	2·74	− 3	
	11 a.m.–3 p.m.	92	0·0536	0·163	3·04	+ 8	
	3–7 p.m.	280	0·0716	0·213	2·97	+ 5	
	7–10 p.m.	69	0·1089	0·254	2·33	−18	
2	As above	34	0·0546	0·134	2·46	+ 1	+25
		50	0·0643	0·155	2·41	− 1	
		37	0·0609	0·236	3·88	+60	
		(10	0·0273	0·072	2·64	+ 8)	
		39	0·0721	0·179	2·48	+ 2	
3	,, ,,	29	0·0611	0·189	3·10	+ 5	+53
		189	0·0685	0·194	2·83	− 5	
		284	0·0707	0·362	5·12	+73	
		113	0·0687	0·322	4·69	+59	
		207	0·0797	0·276	3·46	−17	
4	,, ,,	66	0·0758	0·287	3·79	− 2	+ 1
		74	0·0809	0·316	3·91	+ 2	
		94	0·0610	0·298	4·89	+27	
		66	0·0845	0·295	3·49	− 9	
		43	0·0501	0·156	3·11	−19	
5	,, ,,	21	0·0481	0·138	2·87	+ 3	+46
		35	0·0421	0·114	2·71	− 3	
		109	0·0578	0·275	4·77	+71	
		16	0·0582	0·239	4·11	+48	
		25	0·0693	0·214	3·09	+11	
6	,, ,,	77	0·0603	0·246	4·08	+ 3	+ 6
		198	0·0628	0·241	3·83	− 3	
		256	0·0734	0·416	5·67	+44	
		61	0·0827	0·271	3·28	−17	
		123	0·0804	0·278	3·45	−13	
7	,, ,,	58	0·0580	0·208	3·59	+ 1	+51
		118	0·0796	0·281	3·53	− 1	
		149	0·0633	0·388	6·13	+72	
		38	0·0699	0·407	5·82	+64	
		59	0·0922	0·352	3·82	+ 7	
8	,, ,,	150	0·0848	0·126	1·49	−24	+ 7
		63	0·0545	0·133	2·44	+24	
		183	0·0548	0·121	2·21	+12	
		77	0·1149	0·261	2·27	+16	
		59	0·0802	0·142	1·77	−10	
9	,, ,,	29	0·0831	0·481	5·79	+21	+39
		30	0·0491	0·186	3·79	−21	
		61	0·0541	0·384	7·09	+48	
		2	0·0043	0·009	6·43	+34	
		27	0·0946	0·626			
10	,, ,,	55	0·0666	0·194	2·92	+ 4	+ 6
		174	0·0610	0·163	2·67	− 4	
		146	0·0735	0·184	2·50	−11	
		80	0·0548	0·182	3·32	+19	
		37	0·0748	0·232	3·10	+11	

* Weighted to allow for difference in lengths of periods.

subsequently. The patients were not subject to any special degree of control, and losses of urine were suspected, since the volumes collected varied considerably from day to day.

The average excretion of H.I.A.A. in the group appeared to be slightly above the average on the first day of the investigation and on the first day after reserpine; this indicated that the reliability of the collection declined after the first 24 hours, but also suggested that there might be a slight increase in H.I.A.A. excretion following the first dose of reserpine.

In an attempt to obtain more positive results, tests were carried out on four normal subjects, each given a single dose of 5 mg. of reserpine. The plan of the collection differed only in detail from the standardized test subsequently adopted. In the last of these the estimation of creatinine as well as H.I.A.A. was introduced, following the principle of Snow *et al.* (1955). An increase in H.I.A.A. excretion was observed in three out of the four cases; the relating of the H.I.A.A. to creatinine gave the response a more regular form (see below). This series was then completed by tests on six patients.

A review of the results indicated that 6 out of these 10 subjects had shown increased excretion of H.I.A.A. following reserpine, particularly during the first four hours. These had also exhibited a marked diuresis, while others had not. Tests were therefore carried out to determine whether the latter could by itself account for the rise in H.I.A.A. They indicated that it could not, but at the same time demonstrated that the method of estimation was not recovering 100% of the H.I.A.A. from concentrated urines. This point was investigated in some detail, and fully confirmed, without any specific cause being found; however, adequate dilution appeared to provide a practical solution to the problem and the method described in the previous section of taking a fixed fraction of the urine specimen was finally adopted.

Results in Final Series

The results of the tests on the final series of 10 selected patients are given in Table I. The hourly rate of urine excretion varied from 2 to 284 ml. in the group; even neglecting the smallest specimen, there were two rates of under 20 and four of over 200 ml./hr., and the individual ranges in rate exceeded fourfold in the majority of cases, being nearly tenfold in two.

It had previously been noticed that reserpine appeared to cause a diuresis which was followed by a reduction of the fluid output to an inconveniently low level in the later stages of the test; it was therefore arranged that patients should be given ample fluid during the afternoon. However, the weather during the investigation included a number of unusually hot days which caused an abnormally high loss of water by perspiration in some cases (in particular in the period for which the 2 ml./hr. rate was observed). Accidental loss (about 10 ml.) was reported on one occasion.

The means and ranges of the volumes excreted in the several periods of the test are given in Table II.

TABLE II.—*Rates of Urine Excretion*

Period	Mean Rate of Excretion (ml. hr.)	Range
10 p.m.–7 a.m.	54·8	21–150
7–11 a.m.	97·7	30–198
11 a.m.–3 p.m.	141·1	37–284
3–7 p.m.	74·3 (91·4)*	2–280 (16–280)*
7–10 p.m.	68·8	25–207

* Omitting two lowest figures (see below).

Diuresis, therefore, was again observed in the period following the injection of reserpine. There was a tendency for the rate of urine excretion to be somewhat reduced in the second and third periods despite the measures taken to maintain it.

Low rates of excretion could reduce the total amount of solids excreted during a period, including the amounts of creatinine and H.I.A.A. Since creatinine excretion is regarded as being fairly steady under normal conditions, and since, as is shown above, the variations during the 24 hours were not great, the creatinine excreted in small volumes has been compared with that excreted in the other periods by the same individual; in the 2 and 10 ml./hr. specimens the amounts were abnormally low, but in the next smallest specimens, 16 and 21 ml./hr., the amounts excreted were within the range for the individual.

The creatinine excretion had been measured in the first instance as a check on the reliability of the urine collection and subsequently in order to be able to determine the H.I.A.A./creatinine ratio, which appeared to improve the regularity of the results. Any change in this ratio could be due to a change in either the H.I.A.A. or the creatinine excreted, or in both; the figures for creatinine have therefore been analysed to determine to what extent their variation could account for any alteration of the ratio. The mean creatinine levels in each period are shown in Table III. The figures show that there is a negligible fall in the mean creatinine level in the first period after reserpine, by comparison with the observed rises in the H.I.A.A./creatinine ratio, and that during the second and third periods there is an actual rise in the creatinine level which would, in fact, tend to reduce the ratio.

TABLE III.—*Mean Creatinine Excretion*

Period:	10 p.m.–7 a.m.	7–11 a.m.	11 a.m.–3 p.m.	3–7 p.m.	7–10 p.m.
Creatinine excretion (mg. hr.)	65·5	63·9	62·4	75·9	80·2
" " —percentage change	—	—	−4	+17	+24

There remains, however, the possibility that the patients showing an increase in H.I.A.A./creatinine ratio in response to reserpine do so by reason of their exhibiting an equal and opposite change in creatinine excretion from the unresponsive patients. An analysis of this possibility is given in Table IV.

TABLE IV.—*Creatinine Excretion According to Response to Reserpine*

Period:	10 p.m.–7 a.m.	7–11 a.m.	11 a.m.–3 p.m.	3–7 p.m.	7–10 p.m.
Positively responding Group (4):					
Creatinine (mg. hr.)	62·5	60·0	61·5	65·7	84·0
" —percentage change	—	—	±0	+7	+37
Unresponsive Group (5):					
Creatinine (mg. hr.)	70·2	67·0	63·4	82·0	78·8
" —percentage change	—	—	−8	+19	+15

While the numbers in each group are small, it seems that, owing to changes in creatinine output, the ratio for the unresponsive group would increase more than that for the positively responding group during the first four hours after reserpine; this would be counterbalanced by a smaller decrease in the ratio for the positively responding group during the second four hours; the overall effect favours a relative rise in the ratio of the unresponsive group. The observed trends in H.I.A.A./creatinine ratio are therefore quite independent of changes in creatinine excretion following reserpine.

It has previously been suggested that the analysis of the results in terms of the H.I.A.A./creatinine ratio rather than in terms of H.I.A.A. excreted per hour leads to a greater regularity in the results. *A priori*, the actual hourly excretion might be preferred on the grounds that it is a direct estimate, but the ratio does make allowance for one possible and not easily recognizable cause of error—namely, loss or retention of urine.

One test of the alternative methods of handling the data has been to compare the estimates obtained from the two pre-reserpine periods. Four times there were considerable

differences between these estimates, twice with each method; these involved three cases. In the remaining seven cases the differences were relatively small, but the mean percentage difference in H.I.A.A. per hour was 10.9, whereas the mean percentage difference in the ratio was less than two-thirds of this figure (6.0).

The maximum increase in H.I.A.A per hour after reserpine occurs five times in the first period, twice in the second, and thrice in the third, whereas the maximum increase in the ratio occurs eight times in the first and twice in the second period.

The mean percentage increase in H.I.A.A. excretion for the whole 11 hours following reserpine has been calculated by both methods, and is given in Table V.

TABLE V.—*Mean Percentage Increase in H.I.A.A. Excretion Following Reserpine*

Case No.:	1	4	10	6	8	2	9	7	3	5
Mean percentage increase:*										
5-H.I.A.A.(mg. hr.) ..	+17	+9	+13	+32	+35	+46	+52	+57	+68	+94
.. (mg./g. creatinine)	±0	+1	+6	+6	+7	+25	+39	+51	+53	+46
Classification of response	−	−	−	−	−	±	+	+	+	+

* For three periods following reserpine injection.

The mean percentage change in H.I.A.A. excretion per hour forms a broad spectrum of values, while the H.I.A.A./creatinine ratio figures fall more clearly into two groups, the absolute values of which, 0 to +7 and +39 to +53, can justifiably be equated to negative and positive responses. Division of the H.I.A.A./hr. figure into two types of response would be possible, but more than one arbitrary division could be made.

The H.I.A.A./creatinine ratio having been adopted, the results of the tests on the response of humans to reserpine can be summarized as follows. There have been no examples of significant depression of H.I.A.A. excretion following reserpine, but about half the cases have responded to 5 mg. intramuscularly by a clear-cut increase in H.I.A.A. excretion.

The fact that the response is not always present is evidence against any suggestion that H.I.A.A. excretion normally rises after midday; there is also direct evidence to indicate that it varies little throughout the 24 hours (Table VI).

TABLE VI.—*Diurnal Variation in H.I.A.A. Excretion (mg./hr.)*

Subject	7–11 a.m.	11 a.m.–3 p.m.	3–7 p.m.	7–11 p.m.	11 p.m.–7 a.m.
A* ..	0·29	0·25	0·25	0·22	0·21
B ..	0·22	0·21	0·24	0·25	0·24
C ..	0·26	0·26	0·28	0·29	0·25

* Collection in this case was 8.30–8.30 a.m.

This investigation was concluded by comparing the response of the patient to reserpine with the psychiatric diagnosis and with certain other psychiatric and clinical parameters. It has been considered justifiable to include the previous series of cases in this comparison, since the experimental data are regarded as probably adequate in most instances for the assessment of positive or negative responses.

TABLE VII.—*Comparison of Response to Reserpine with Diagnosis*

	Response	
	Negative	Positive (and Doubtful)
1st series	Normal	Normal
	Schizophrenic	..
	..	..
	Depressive	Schizophrenic
		Chronic anxiety state
		Inadequate psychopath (? M.D.)
2nd series	Schizophrenic	Schizophrenic
	..	..
	Aggressive psychopath	..
	Alcoholic	Aggressive psychopath
	..	Anxiety state

From Table VII it can be seen that these responses did not differentiate between schizophrenic and non-schizophrenic diagnoses. Similarly, the response was not related to subtype of schizophrenia, to primary thought disorder, or to gross secondary symptoms in schizophrenia, nor, in the group as a clinical whole, to age, height, weight, height/weight ratio, blood pressure, duration of psychiatric process, or the presence of symptoms of tension.

Discussion

Our preliminary observations broadly confirmed those of Haverback *et al.* (1956b) that there was no significant rise in the 24-hour urinary H.I.A.A. excretion following reserpine. Subsequent tests, however, indicated that there was a rise in H.I.A.A. excretion in about half the cases which was maximal in the first four hours after the injection and had fallen to about one-sixth of the maximum between the eighth and eleventh hours. It is not possible to say whether the excretion would later have fallen below normal, though it is perhaps worth noting that two of the five cases showing negative responses did so as the result of a transient rise being counterbalanced by lower than normal excretions during the second and third periods.

In the animal experiments the 400% increase observed was regarded as coming largely from the intestinal stores of H.T. (Shore *et al.*, 1955); since these are thought to be more resistant to mobilization by reserpine than other sources (platelets, brain, spleen) it is of interest to calculate whether the platelet H.T. could adequately account for our observed increase in H.I.A.A.

In the group showing a positive response, the mean increase in H.I.A.A. excretion over the control level totalled 1.2 mg. for the 11-hour period. There was a slight increase in the unresponsive group, 0.2 mg., which could be deducted, leaving 1 mg. to be accounted for.

A recent figure for the H.T. content of whole blood is 0.16 ± 0.06 μg./ml. (Hardisty and Stacey, 1955); on the assumption that the blood volume is 8% of the body weight, this gives the normal range for the total blood H.T. as 0.8 ± 0.3 mg.

Summary

The H.I.A.A. excretion of four normal subjects and 16 mental patients has been studied before and after an intramuscular injection of 5 mg. of reserpine.

An increase was observed in half the subjects; this was maximal and of the order of 60% of the control level over the first four hours; it remained high during the second four hours; but thereafter was hardly significant.

The responsiveness or otherwise of the patients to the drug does not correlate with the psychiatric diagnosis.

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BODY WATER IN EPILEPSY*

BY

OSCAR OLBRICH, M.D., Ph.D., F.R.C.P.Ed.†
Consultant Physician

E. WOODFORD-WILLIAMS, M.D., M.R.C.P.
Late Assistant Physician

A. GILLIS, M.R.C.P.Ed., D.P.M.
Consultant Psychiatrist

AND

E. C. ATTWOOD B.Sc.
Biochemist
Geriatric Unit, the General Hospital, Sunderland

Epilepsy, one of the first maladies to be described, still remains a subject for investigation. Experimentally, fits have been produced in animals by overhydration and controlled by dehydration. Moreover, dehydration has been used with some success as a therapeutic measure in epilepsy, the electroencephalogram showing improvement as a result.

Although previous work indicates that disturbance of body fluid distribution plays an important part in the production and prevention of fits, the relation between the distribution of extracellular water and total body water in epilepsy is not so well established. In the present work, with the object of elucidating this problem further, a comparison has been made of the values found for extracellular water and total body water in a group of epileptic and non-epileptic subjects in the same age range.

All those investigated were males whose ages ranged from 18 to 66 years, 18 were epileptic and 38 non-epileptic. In the epileptics the length of history varied from 2½ to 40 years.

The subjects were prepared for the test by giving a low protein diet and ample fluid the day before. On the morning of the test, after recording the height and weight, a self-retaining catheter was passed, the bladder emptied completely, and the time noted. The urine was discarded and all further samples were related to this zero time.

Methods

Total body water was measured by the urea method (McCance and Widdowson, 1951). In 17 patients we found good agreement (r = 0.94) between this method and that using N.A.A.P. (N-acetyl-4-aminoantipyrine) (Brodie *et al.*, 1949), measurements with N.A.A.P. having been found to correspond closely with those made with deuterium oxide. The extracellular space was measured with sodium thiosulphate (Cardozo and Edelman, 1952). When this method was compared with inulin for measurement of extracellular space, the correlation was also highly significant (p = 0.96). Serum sodium was estimated by flame photometry.

Measurement of Extracellular Space.—A blank sample of 10 ml. of venous blood is collected, the skin having been anaesthetized with 2% procaine solution. An intravenous drip of 1 litre of 5% dextrose in water is then set up to run at 120 drops per minute. Into the tubing of the drip is injected 10 g. of 50% sodium thiosulphate, taking 10 minutes over the injection. The exact time is noted at the beginning and on completion of the injection. A further 100–120 ml. of glucose is then run through the drip at the same rate to wash through the sodium thiosulphate; thereafter the drip can be dismantled. Blood samples, taken if possible without venous stasis, are collected through a heparinized Gordh needle, at 10-minute intervals, rejecting the first 2 ml., the first sample being taken 10 minutes after the injection of sodium thiosulphate.

Urine samples are collected at 30, 60, and 90 minutes after the injection for determination of thiosulphate excretion rate and for use as blanks in the determination of basic urea excretion rate for estimation of total body water.

Measurement of Total Body Water.—As soon as the two blank urine samples have been collected, 2.5 g. of urea per stone (0.4 g. per kg.) body weight is given orally. The time is noted when all the urea has been taken. Urine is collected 90, 150, and 210 minutes after giving the urea, and venous blood samples are taken half-hourly for two hours to ensure that the peak concentration of urea in the blood is obtained, thereafter one or two more blood samples are taken at hourly intervals.

Results

The mean weight of the epileptic subjects was 65.6 kg. and of the non-epileptics 64.0 kg.

The mean total body water, expressed as percentage of body weight, was 70.3% ± 7.7%, with a range of 50.1–86.4%, in the non-epileptics (Table I), and 66.6% ± 7.5%, with a range of 52.4–84.8%, in the epileptics. According to Student's "t" test this difference between the means is not significant (p = 1.75). The mean value for extracellular water, expressed as percentage of body weight, in the non-epileptic group was 17.8% ± 3.1%, with a range of 15.3–23.8%, and in the epileptic group 19.4% ± 3.7%, with a range of 13.3–28.7%. The difference is not significant (p = 1.74).

TABLE I.—*Extracellular Water (Litres) and Total Body Water (Litres) as Percentage of Body Weight (kg.) in Normal and Epileptic Subjects*

		Normals (38 Cases)	Epileptics (18 Cases)	"t" Test
E.C.W. % Body wt.	Mean	17·8 S.D. ± 3·1	19·4 S.D. ± 3·7	p = 1·74. Not significant at 0·05 level
	Range	15·3–23·8	13·3–28·7	
T.B.W. % Body wt.	Mean	70·3 S.D. ± 7·7	66·6 S.D. ± 7·5	p = 1·75. Not significant at 0·05 level
	Range	50·1–86·4	52·4–84·8	

Absolute values for total body water also do not differ significantly in the two groups (Table II). In the non-epileptics the mean for total body water was 44.9 l. ± 6.4 l., range 32.1–60.3 l., and in the epileptics the mean was 43.4 l. ± 6.8 l., the range being 35.1–53.6 l. The difference between the absolute values for extracellular water was found to be significant. In the normal group the extracellular water in litres measured 11.3 ± 1.76, with a range of 7.9–15.1 l. In the epileptics the mean was 12.5 l. ± 3.1 l., with a range of 10.6–18.0 l., the difference being significant at the 0.05 level (p = 2.3).

TABLE II.—*Extracellular Water and Total Body Water in Normal and Epileptic Subjects*

		Normal (38 Cases)	Epileptics (18 Cases)	"t" Test
E.C.W. (litres)	Mean	11·30 S.D. ± 1·76	12·49 S.D. ± 3·1	p = 2·3. Significant at 0·05 level
	Range	7·9–15·1	10·6–18·0	
T.B.W. (litres)	Mean	44·9 S.D. ± 6·4	43·4 S.D. ± 6·8	p = 0·8. Not significant
	Range	32·1–60·3	35·1–53·6	

When the ratio of extracellular water to total body water expressed as a percentage was compared in the non-epileptic and epileptic groups, the significance of the difference between the two groups becomes more evident (Table III). In the non-epileptic group the mean E.C.W./T.B.W.% was

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†Dr. Olbrich died on August 22, 1957.

TABLE III.—*Extracellular Water (Litres) as Percentage of Total Body Water (Litres) in Normal and Epileptic Subjects*

		Normal (38 Cases)	Epileptics (18 Cases)
E.C.W.% / T.B.W.%	Mean	25·3 S.D. ± 3·4	29·0 S.D. ± 5·1
	Range	18·9–32·8	22·7–35·9

"t" test: p = 3·7. Significant at 0·01 level

25.3 ± 3.4, range 18.9–32.8, whereas in the epileptics it was 29.0 ± 5.1, range 22.7–35.9. This difference is significant at the 0.01 level (p = 3.7).

Of the epileptic patients 10 were in the age group 18–45 and 8 were between the ages of 46 and 66 (Table IV). The mean E.C.W./T.B.W.% in the 10 epileptics aged 18–45 was 29.7, range 22.7–35.9, and in the 8 aged 46–66 it was 29.2, with a range of 24.5–32.6. No significant difference was found between the means in these two age groups.

The epileptics have also been grouped according to the frequency of fits: six had fits once a week to once a month, eight had fits once every few months, and four had fits

TABLE IV.—*Extracellular Water (Litres) as Percentage of Total Body Water (Litres) in Epileptics Aged 18–45 Years and 46–66 Years*

		Epileptics Aged 18–45 Years (10 Cases)	Epileptics Aged 46–66 Years (8 Cases)
E.C.W.% / T.B.W.%	Mean	29·7	29·2
	Range	22·7–35·9	24·5–32·6

"t" test: p = 0·124. Not significant at 0·05 level.

TABLE V.—*Extracellular Water (Litres) as Percentage Total Body Water (Litres) in Epileptics With (a) Frequent Fits, (b) Moderately Frequent Fits, and (c) Infrequent Fits*

		Group A (6 Cases)	Group B (8 Cases)	Group C (4 Cases)
E.C.W.% / T.B.W.%	Mean	32·5	28·2	25·0
	Range	31·0–33·6	22·7–35·9	23·8–27·5

"t" test (A–B): p = 2·7. Significant at 0·02 level.
"t" test (A–C): p = 3·9. Significant at 0·01 level.

rarely (Table V). In these groups the mean value found for E.C.W./T.B.W.% was 32.5, 28.2, and 25.0 respectively. Applying the "t" test, a significant difference was found at the 0.02 level (p = 2.7) between the means of the group with frequent fits and the group with moderately frequent fits, and a more highly significant difference at the 0.01 level (p = 3.9) was found when the group with frequent fits was compared with the group who rarely had fits or with normals.

The average total sodium in the extracellular space of epileptic and non-epileptic patients was 1,416 and 1,216 mEq respectively.

Comment

For comparative study, data concerning body fluid measurements are usually related to body weight or surface area; that this is not satisfactory, owing to the individual variation in fat mass, is discussed in other work under preparation. A more accurate baseline is the lean body mass.

Pace and Rathbun (1945) have shown that, irrespective of the species of animal investigated, the total body water calculated on a fat-free basis is approximately constant at 73%. From this it follows that the lean body mass (fat-free) can be calculated from the total body water (T.B.W./0.73 = L.B.M.). As the lean body mass bears a constant relationship to the total body water, the ratio E.C.W./T.B.W. should provide a more valuable index of normality in regard to body fluid distribution than data related to body weight, in which the relatively anhydrous fat mass comes into consideration.

Our findings confirm this observation; thus when values for extracellular water in the epileptic and non-epileptic series are related to body weight no significant difference was found between the means of the two groups owing to the fact that the epileptic patients were, on average, 1.6 kg. heavier than the non-epileptic subjects.

The ratio E.C.W./T.B.W., however, was found to be significantly different in the epileptics as compared with the non-epileptics; moreover, this difference was more significant in the epileptics with frequent fits, indicating a greater increase in extracellular water in these patients as compared with those who had fewer seizures. Age was not a factor in producing this change.

The significant difference found in the absolute quantity of extracellular water, and in the ratio E.C.W./T.B.W., between the epileptic and non-epileptic group was not due to a difference in the "variance ratio" in the two groups, and can be regarded as representing a real increase of extracellular fluid in epileptic patients as compared with non-epileptic subjects. Since the total body water in litres does not differ significantly in either group, there must also be a relative intracellular dehydration in the epileptics, the degree varying with the amount of extracellular water.

The total increase of sodium found in the extracellular fluid in the epileptic group is associated with the increase of fluid in the extracellular space in epileptics as compared with the non-epileptics.

As all the epileptics were investigated in the interval between attacks our results suggest that an increase of extracellular fluid is always present in epileptics, and it is this which predisposes them to seizures, a finding which is in agreement with the observation of Dandy (1923), who noted in chronic epilepsy abnormal deposition of fluid, especially over the frontoparietal areas of the brain. Furthermore, Pancoast and Fay (1929), in encephalographic studies on epileptics, also found increase of supracortical fluid to be a constant feature in the well-established case of epilepsy.

The beneficial results reported from treatment such as starvation (Guelpa and Marie, 1911), dehydration (Gamble, 1930; Fay, 1930), ion-exchange resins (Klingman, 1954), and acetazolamide (Ansell and Clark, 1956), which probably also depend to some extent on the loss of fluid and sodium from the extracellular space, add further support to our findings.

In conclusion, as an increase of extracellular fluid has been found a constant feature in epilepsy, it would seem that restriction of sodium in the diet is a rational approach in the treatment of this malady.

Summary

The total body water and extracellular water has been measured in 18 epileptics and 38 non-epileptic patients. The total body water did not differ significantly in the two groups. A significant difference was found in the amount of extracellular water, and in the ratio E.C.W./T.B.W. in epileptics as compared with non-epileptics. There is a relative intracellular dehydration in epileptics. The significance of these findings in relation to treatment is commented upon.

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NITROUS OXIDE ANAESTHESIA WITHOUT HARM

BY

J. W. MOSTERT, M.B., Ch.B., D.A., F.F.A.R.C.S.
Anaesthetic Registrar, Worthing Group of Hospitals

Although evidence has been presented showing that the anaesthetic effect of nitrous oxide is not produced by and need not be accompanied by anoxia, it is equally certain that 85 to 90% of this gas is required in the inhaled atmosphere to produce anaesthesia. It follows that the 20.93% oxygen present in the surrounding air cannot be allowed if the anaesthesia is to be of short duration. The fact, perhaps not so well known, that anaesthesia produced solely by nitrous oxide is possible and practical without hypoxia is the subject of this paper.

The Physiological Basis

Normally the effective tidal volume is of the order of 300 ml., while the total effective lung volume after normal inspiration is equal to this volume plus the functional residual capacity, some 2.8 litres in all. Respiration, being a cyclical process, thus causes the anaesthetic gas inhaled in the first breath to be diluted in a considerable lung volume containing no anaesthetic gas, but only 14.2% oxygen and 80% nitrogen. It is therefore apparent that after the administration of pure nitrous oxide begins a precipitous drop in this 14.2% oxygen must occur, with anoxic anoxia. If, however, the nitrogen is replaced by oxygen before induction of anaesthesia, the same precipitous decline in oxygen concentration must occur, but at least the gradient then begins at 100% instead of 14.2%. Ninety-eight per cent. of "washing out" of nitrogen can actually be accomplished by administration of pure oxygen for merely two minutes, except in cases of grossly uneven distribution of the inspired gas, such as obtains in advanced pulmonary emphysema (Comroe *et al.*, 1955).

More precisely, oxygen diffuses across the pulmonary epithelium normally under a partial pressure of about 60 mm. Hg. After breathing pure oxygen for a few breaths the gradient will be around 600 mm. Hg. On the basis of a functional capacity of 2,500 ml. some 1,800 ml. of oxygen could then be absorbed or eliminated via the tidal air before the oxygen tension in the alveoli would fall to the normal level of 100 mm. Hg.

Miles, Martin, and Adriani (1956) and Hamilton and Eastwood (1955) studied the elimination of nitrogen from the lungs of healthy volunteers breathing oxygen from semi-closed inhalers used in anaesthesia. The former group of workers confirmed that at flow rates equal to the minute-volume exchange of the subject, with no rebreathing, elimination occurred at an average of two and a half minutes. Hamilton and Eastwood found, as expected, that the rate of nitrogen elimination is affected by the rate of flow of gases more than by the system used, and concluded that there appeared to be no clinical advantage in the use of gas flows above 4 litres per minute for the purpose of nitrogen elimination.

Another advantage of preliminary oxygenation is suggested by a comparison of the speed of diffusion of the relevant gases. An isolated lung lobule filled with nitrogen whose bronchus is occluded requires some 16 hours for the nitrogen to diffuse into the blood and for complete deflation of the lobule. Under similar circumstances oxygen disappears in 15 minutes and nitrous oxide in 17 to 35 minutes (Adriani, 1946). This may account for my experience that anaesthesia induced with pure nitrous oxide after preliminary oxygenation is more prompt and profound than in the absence of preliminary oxygen breathing. Again, these considerations apply only to the healthy, Comroe *et al.* (1955) listing various diseases of the lungs which secondarily or specifically impair diffusion.

Finally, a change from the inhalation of 20.93% oxygen to 100% increases the oxygen content of normal blood by a total of 2.2 volumes% or 11% of the total (Comroe and Dripps, 1950). Firstly, the saturation of haemoglobin is increased from 97.5 to 100%, adding 0.5 volume% of oxygen in combination with haemoglobin. Secondly, an additional 1.7 volumes% of oxygen is dissolved in the blood.

Under these conditions, despite the administration of pure anaesthetic gas, perfect oxygenation is assured for 30 to 45 seconds, 6 to 10 respirations, by virtue of the reservoir of oxygen present in the lungs and blood.

Pure nitrous oxide administered for 40 to 60 seconds, or 16 to 20 breaths, is ample for the production of the state of anaesthesia in the healthy. This view can be verified without harm in as many seconds by anyone who wishes to do so. Kety (1951) discussed in great detail the theory and applications of the exchange of inert gas at the lungs and tissues, and the physiological factors more simply elsewhere (Kety, 1950). With every anaesthetic agent the various stages of anaesthesia are associated with definite concentrations of the anaesthetic agent in the brain, and, provided equilibrium has been attained, with definite concentrations in the blood. With a number of gases, including nitrous oxide, the concentrations in blood and in whole brain have been found to be approximately equal. The problem of the rate of induction is thus reduced to the solubility, or rate of uptake, of the anaesthetic gas by the blood. As already indicated, the relatively small and lipid-soluble molecules of nitrous oxide diffuse very rapidly across cell membranes. Thus, gas in the alveoli equilibrates practically instantaneously with blood passing through the pulmonary capillary bed. This has been established by careful physiological studies, most recently by the use of radioactive gases.

The solubility of nitrous oxide, or the ratio of the concentration of dissolved gas to the concentration in the gas phase, at equilibrium is quite low—namely, 0.47. Therefore the major physiological factor limiting equilibration is the cardiac output rather than the respiration, as is the case with high-solubility agents like ether (15.0). The blood is already carrying all the anaesthetic it can for a given partial pressure of gas, and only a small fraction is removed by the blood at each breath, while at the next breath even this is replenished. And this is the only site where the anaesthetist can exert control by providing maximal "driving force," or "pressure head," of gas. For nitrous oxide is such a mild anaesthetic agent that it must be given in high concentration during induction if the excitement stage is to be avoided and smooth anaesthesia is to be produced.

The word "saturation" is often incorrectly used in this connexion, the word "equilibrating" being more satisfactory in describing approximation of body and fat anaesthetic concentration to a given alveolar anaesthetic concentration. It is said that if the blood carries a fixed and safe concentration of nitrous oxide away from the lungs, the cardiac output being 5 litres per minute and the total body water about 45 litres, it follows that the latter can be brought to equilibrium only in a minimum of nine minutes; and in view of the asymptotic nature of the process (blood returning to the lungs will soon contain some anaesthetic, diminishing the net transfer) the calculated time for 90% equilibrium of the whole body must be much more—approximately 21 minutes (Kety, 1951).

Organs such as the heart and brain are, however, richly supplied with blood. Thus the blood supply to the brain has been found to be about 350 ml. per kg. per minute, while the mean figure for the rest of the body water is approximately 100 ml. per litre per minute. Equilibration in the brain can therefore be expected to occur about 3.5 times faster for brain than for body water as a whole, the observed time of about seven minutes for 90% equilibration being in accord with the theory. Gray (1954) provided experimental evidence that this may be more rapid, and in practice I find that the inhalation of pure nitrous oxide for

one minute invariably provides adequate anaesthesia within the next half-minute. While the rate of equilibration can be expected to be most rapid early on, confirmation of an adequate approximation to equilibrium in the brain after one minute of nitrous oxide inhalation is nevertheless clearly desirable; for on it probably depends the whole future of nitrous oxide anaesthesia in dentistry and out-patient surgery.

It is certainly not necessary for equilibration of the whole body mass to be aimed at. Such a state inevitably occurs with anaesthetics of a high solubility resulting in prolonged induction and recovery, and Fink (1955) has shown this to result in one of the main hazards of prolonged nitrous oxide anaesthesia—the rapid elimination of some 28 litres of anaesthetic gas ensuing at the termination of anaesthesia, providing the necessity, once more, of oxygen therapy to remedy the "diffusion" or dilution variety of anoxic anoxia.

Technical Considerations

As a first step pure oxygen is administered at a flow rate of 10 litres or more per minute for two minutes. The patient is previously instructed to breathe normally via a tight-fitting nose- or face-piece. Pure nitrous oxide subsequently administered for one minute, at a flow rate similarly well in excess of the minute-volume and without rebreathing, will produce surgical anaesthesia in all healthy patients. Breath-holding is very rare with nitrous oxide as opposed to cyclopropane. At least 20% oxygen is then added as well as supplementary agents if the surgeon requires more than two to three minutes for the operation. If supplementary agents are not used anaesthesia will lighten during this period. It is interesting that Tom (1956) regards this stage, resulting after breathing 20% oxygen with nitrous oxide, still suitable for dental surgery in older children and adults. Certainly, less than 20% oxygen cannot safeguard against harmful anoxia if it is remembered that the average administrator of nitrous oxide is not an expert.

I have used this technique for over two years. Dental surgeons and casualty officers have appreciated the apparent lack of anoxia, nausea, and delirium. No premedication is used, but emptiness of stomach, bowel, and bladder is desirable.

The technique is useful in allowing time for patients to become accustomed to the apparatus while the anaesthetist carries on a monologue keeping the patient informed that he is not expected to feel any effect during the prelude of oxygen therapy. A few patients who had previous experience of nitrous oxide anaesthesia suggested that this technique removed the unpleasant sensations associated with increasing anoxia, and personal experimentation confirmed this admittedly biased impression.

My attention has been drawn to three facts which, if not mentioned, may allow the method to fall into disrepute. They are: (1) After administering pure nitrous oxide for one minute I habitually allow (except in obstetrics) merely 10–15% oxygen for 15–30 seconds, during which time the surgeon is generally able to embark on his operation without having to contend with a moving patient. Only then do I very carefully administer at least 20% of oxygen. (2) A single breath of air early on, such as during the switchover to anaesthetic gas, may vitiate the advantage gained by this method to a remarkable extent. This point cannot be overemphasized. (3) The astute may economize by using merely 4 litres of oxygen per minute for the purpose of nitrogen elimination. This will, however, result in some carbon dioxide accumulation.

Conclusions and Summary

A technique of nitrous oxide anaesthesia for brief operations in healthy subjects is described. It depends simply on routine nitrogen "washout" by administration of pure oxygen for two to two and a half minutes prior to the administration of pure nitrous oxide. Further reasons are advanced why this technique may avoid anoxia and, incidentally, nausea and delirium, provided that the inherent limitations of nitrous oxide as a sole anaesthetic agent are observed. Except in expert hands, there must be strict limitation of the time spent on surgery, unless recourse is made to supplementary agents or a state of amnesia and analgesia such as results after the inhalation of 20% oxygen in nitrous oxide.

The idea of nitrogen elimination and its replacement by oxygen prior to nitrous oxide anaesthesia is not new (Neff *et al.*, 1950), but its overall importance appears to be overlooked in practice.

I am indebted to Dr. F. R. Gusterson for advice and encouragement.

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ACUTE RENAL FAILURE IN SALICYLATE POISONING

BY

E. J. M. CAMPBELL, M.D., M.R.C.P.
Assistant

AND

R. E. MACLAURIN, M.B., B.S.
Late House-physician

Medical Unit, the Middlesex Hospital, London

Salicylate poisoning causes complex acid-base and metabolic disturbances. If serious renal damage is present in addition, as in the following case, the management demands careful biochemical control.

Methods.—The plasma sodium and potassium concentrations were measured by flame photometry, the chloride by the method of Van Slyke and Hiller (1947), the bicarbonate by the method of Van Slyke and Neill (1924), and the salicylate by the method of Smith and Talbot (1950). The arterial carbon dioxide and oxygen tensions were measured by the Riley method (Riley, Campbell, and Shepard, 1957) and the *p*H calculated from the nomogram of Singer and Hastings (1948).

Case History

On February 13, 1957, a spinster of 52 swallowed 75 aspirin tablets—total dose approximately 375 gr. (25 g.). Throughout February 13 and 14 she became increasingly drowsy, but remained rousable and was drinking adequately but passing little or no urine. She did not vomit. She was referred to hospital at midday on February 15. There was no previous history suggestive of renal disease.

On admission she was drowsy and confused but responded to simple questions. Her oral temperature was 98° F. (36.6° C.), pulse 105. She was breathing deeply at a rate of 32 a minute. The blood pressure was 100/70; all her extremities were warm and she was sweating. There were bilateral subconjunctival haemorrhages and a purpuric rash on the trunk and arms. During the first six hours in hospital she passed 26 oz. (740 ml.) of urine which was acid and contained protein, hyaline and granular casts, and large amounts of salicylates. Gastric washings contained no salicylates. The blood Hb concentration was 13.9 g./100 ml. Results of other measurements are given in the

Table. The prothrombin "concentration" (Quick) was 28% of normal, to correct which 20 mg. of vitamin K_1 was given intramuscularly.

Results of Investigations

	February						
	15	16	17	18	19	20	21
Weight (lb.)		136	126	136	136	135	135
Blood urea (mg. 100 ml.)	255	325	255	183	100	66	39
Plasma sodium (mEq l.)		142	140	150	152	150	145
,, potassium (mEq l.)		3·6	3·0	2·9	5·8	5·0	4·2
Plasma chloride (mEq l.)	108	110	122	110	112	108	112
,, bicarbonate (mEq l.)	13	12	13	23	33	28	25
Plasma salicylate (mg. 100 ml.)	55			< 5			
Plasma salicylate (mEq l.)	3·5			< 0·3			
Arterial *p*H	7·46		7·44				
,, pCO_2 (mm.Hg)	17		18				
,, pO_2 (mm.Hg)	87·5		95				

During the first 12 hours sodium chloride solution (0.45%) and dextrose (2.5%) was given, to a total of 6 pints (3.4 litres) intravenously, together with glucose drinks (4 pints—2.3 litres) by mouth. During this period she passed 2½ pints (1.4 litres) of urine, but her blood urea rose from 255 to 325 mg./100 ml. (see Table).

February 16.—She appeared much brighter and was drinking freely. Intravenous fluids were therefore discontinued and glucose drinks in 0.45% sodium chloride were given. However, later in the day and during the night she became less co-operative, refused to drink, and developed diarrhoea and urinary incontinence.

February 17.—In view of the loss of weight and clinical evidence of further dehydration intravenous therapy was restarted, again with 0.45% sodium chloride and 2.5% dextrose. Ten pints (5.6 litres) were given in the next 24 hours—this volume being based on the weight loss in the preceding 24 hours. She was also given 125 mEq of potassium (as citrate) by mouth.

February 18.—The patient was clinically much improved. She had gained 10 lb. (4.5 kg.) in weight. There was little clinical evidence of dehydration and the hyperpnoea had ceased. The haemorrhages were absorbing and her mental state was improving. She was, however, weak, and, in spite of the potassium supplement, the plasma potassium concentration had fallen well below the lower limit of normal. The other striking abnormality in the blood chemistry was the persistently raised chloride concentration. As the blood urea had fallen, indicating some return of selective tubular function, and she was now drinking freely, intravenous therapy was discontinued. Glucose drinks in 0.45% sodium chloride were again given. During the next 24 hours she also received 200 mEq of potassium (as citrate) and 400 mEq of sodium bicarbonate.

February 19.—Clinically she was further improved. Her weight was steady and the blood urea had fallen further. It is clear from the other biochemical findings that she had been given too much potassium and probably too much sodium bicarbonate. Unfortunately, the potassium and bicarbonate concentrations were not known at the time and full acid-base studies were not repeated. The raised bicarbonate concentration was probably due to a metabolic alkalosis, but it is not known whether there was an alkalaemia or what respiratory changes there were. The subsequent clinical course was uneventful. Her blood urea returned to normal levels and protein disappeared from the urine. A psychiatrist confirmed a diagnosis of endogenous depression, and she was transferred for psychiatric treatment.

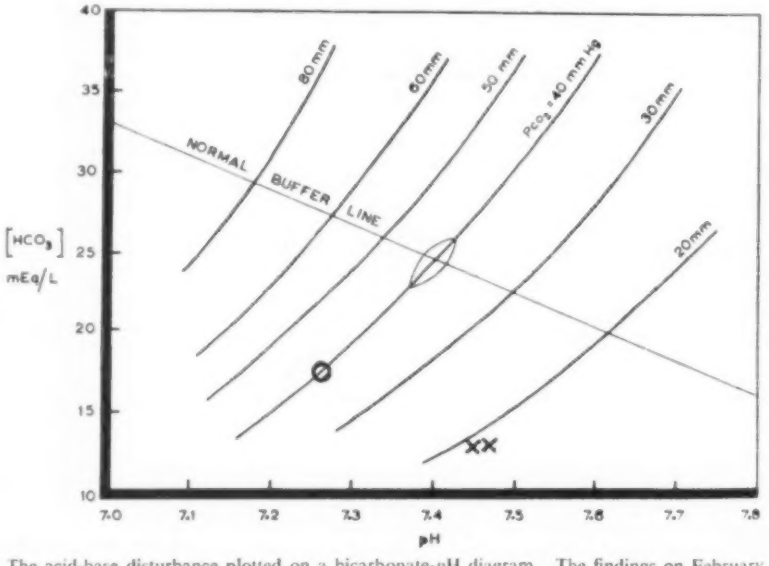
Renal Damage in Salicylate Poisoning

Although at the time of admission the patient was passing large volumes of urine, the rising blood urea and its subsequent fall to normal make the diagnosis of acute tubular failure very probable. An unusual feature was the very high blood urea only 48 hours after taking the salicylate. However, the profound metabolic stimulation produced by salicylates probably accelerated the rate of tissue breakdown to levels much greater than those usually seen in acute tubular necrosis. We were unable to obtain from the patient, her relatives, or her family doctor evidence that would incriminate any agent other than the salicylates as the cause of her renal condition.

Several reports of salicylate intoxication mention the presence of protein and casts in the urine. We were, however, able to find only three cases in which descriptions are compatible with the diagnosis of acute tubular necrosis (Bywaters and Jockes, 1948; Bracey, 1951; Miller, 1955). It would seem possible that some degree of renal damage is commoner than is at present recognized and may play a part in the acid-base disturbance. The possibility should be borne in mind in dealing with patients with salicylate poisoning because the presence of renal damage leads to the retention of salicylate, complicates the acid-base and electrolyte disturbances, and makes treatment more difficult.

The Acid-base Disturbance in Salicylate Poisoning

This subject has been reviewed by Singer (1954). The first effect of salicylate is to cause hyperventilation and a respiratory alkalosis. Some hours later a metabolic acidosis develops, part at least of which is probably due to the accumulation of organic acids. Our patient apparently had entered this stage of combined disturbance when she was admitted to hospital. In the Chart we have plotted her acid-base structure on admission and two days later on a bicarbonate–*p*H diagram (Davenport, 1950) to show the



The acid-base disturbance plotted on a bicarbonate-*p*H diagram. The findings on February 15 and 17 are indicated by ××. The displacement below the normal buffer line represents the metabolic acidosis. The low CO_2 tension represents the respiratory alkalosis. The position on the horizontal scale shows the alkalaemia. The circle indicates the probable conditions if the pulmonary ventilation had been controlled to maintain a normal CO_2 tension.

coexistence of these two defects. It is, of course, not possible on the data available to distinguish between a secondary or compensatory component of the metabolic acidosis and a primary component.

This method of plotting the acid-base disturbance shows that the simple estimation of bicarbonate concentration or alkali reserve in conditions such as these gives insufficient information for proper management. In the present case, the combination of a low bicarbonate concentration and overbreathing could easily have been misinterpreted as indicating a primary metabolic acidosis with acidaemia and have led to the administration of alkali with possibly harmful results.

Treatment

After the first few hours in hospital it was clear that the patient, in addition to having salicylate intoxication, was also in the early diuretic phase of acute renal failure probably due to tubular necrosis. The latter condition required water and electrolyte replenishment, which was given as described above. Attempts to collect full balance data were unfortunately frustrated by the diarrhoea and urinary incontinence. Correction of the acid-base disturbance would have required the administration of alkali to combat the metabolic acidosis, and the reduction of pulmonary ventilation to correct the respiratory alkalosis. Alkali is often recommended because, in addition to combating the metabolic acidosis, it hastens the excretion of salicylates. We withheld alkali in the early stages of treatment because there was an alkalaemia and because the severe renal damage would probably have prevented the rate of salicylate excretion from being significantly increased. It is of interest that in the most authoritative review of the subject Harvie and Singer (1955) doubt the value of alkali administration even in the presence of adequate renal function.

Freier *et al.* (1957) described the case of a patient with salicylate intoxication in whom the respiratory alkalosis was treated by the use of muscular relaxants and artificial respiration to decrease the ventilation. Although they did not estimate the *p*H or pCO_2 the severe tetany of this patient makes it very probable that there was in fact an alkalaemia. It might be inadvisable, however, to use this method simply on the evidence of a high pulmonary ventilation in the absence of good evidence of an alkalaemia. The Chart suggests that if we had acutely reduced the alveolar ventilation to restore the arterial pCO_2 to normal levels (40 mm. Hg) a mild alkalaemia (*p*H 7.46) would have been converted into a more severe acidaemia (*p*H about 7.26).

Fortunately, the clinical progress of our patient and the mild degree of alkalaemia did not demand any specific treatment for the respiratory alkalosis.

Summary

A case of acute renal failure probably due to tubular necrosis following salicylate poisoning is described. A review of the literature suggests that renal damage in salicylate poisoning may be commoner than is generally appreciated and may play a part in the acid-base disturbance. The acid-base disturbance and its bearing on treatment are discussed.

We thank Professor A. Kekwick, under whose care the patient was admitted, for his permission to report this case, and Dr. R. B. Singer for his helpful comments. Many of the investigations were performed by the staff of the routine laboratory of the Courtauld Institute.

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Medical Memorandum

Retroperitoneal Duodenal Rupture

Cohn *et al.* (1952), in a review of 25 cases, estimated that the mortality of retroperitoneal rupture of the duodenum due to blunt force is 20%. Johnson (1944), in a review of the world literature from 1916 to 1944, found only 52 bona-fide cases of retroperitoneal rupture, with a mortality of 50%. Schumacher (1910) and Guibé (1910) gave a mortality of over 90%. The mortality has been falling steadily, no doubt due to more recent methods. When it is considered that the lesion is sometimes discovered only at necropsy and that several series record that it has been missed at laparotomy, there need be no surprise that the mortality remains as it is.

It has been estimated that 10% of all gastro-intestinal ruptures are duodenal and that a quarter of those are retroperitoneal, 90% of the latter affecting the second and third part.

Aetiology

The second part of the duodenum is fixed relatively rigidly by its peritoneal attachments and the third part is vulnerable because it can be compressed against the lumbar spine. Another more theoretical factor in the mechanism of rupture is the blow-out effect: when the pylorus is closed and the duodeno-jejunal angle acute an air trap is formed. The causative forces are many—crush and blast injuries, kicks, traffic accidents, sudden deceleration causing steering-wheel impingement in the epigastrium, etc. The force may be minimal and the causative accident ignored because it was so trivial.

Associated injuries include damage to the liver, spleen, kidney, pancreas, stomach, intestines, omentum, and biliary passages. The lower ribs and transverse processes are often involved and there may be thoracic or more distant skeletal injuries. All these, especially the intraperitoneal lesions, serve to distract the surgeon's attention at the time of operation, and unless signs are fairly gross the duodenal injury may be overlooked.

Diagnosis

The mode of presentation is by no means constant. There is often a paucity of symptoms, and the early course may be benign and insidious. To await overt signs like generalized rigidity may mean the optimum time for intervention has passed. Shock is not usually present, and indeed until the duodenal leak in the retroperitoneum has reached significant proportions symptoms and signs are minimal.

The commonest symptom is abdominal pain, constant and of steadily increasing severity, usually in the right half of the abdomen and often going through to the back. Testicular pain has been described from irritation of the testicular nerves accompanying the spermatic arteries by the retroperitoneal exudate (Butler and Carlson, 1931). Vomiting may come late, and some cases have a minor haematemesis. A rise in temperature and pulse rate may not be evident early. Tenderness and guarding in the right hypochondrium are constant, and, later, rigidity and absent bowel sounds in a larger area indicate peritoneal involvement. Occasionally the crepitation of surgical emphysema in the abdominal or thoracic wall may be felt and pelvic crepitation on rectal examination has been described. There is no constant clinical picture, and only a vigilant awareness and a high "index of suspicion" of the condition enable an early diagnosis to be made. Ancillary investigations provide a useful guide, radiological examination being the most helpful. A plain *x*-ray film of the abdomen can be of the utmost value. This may reveal nothing abnormal, but more often shows free air in the retroperitoneum which may outline the right kidney or present a characteristic "bubble" effect. The retroperitoneal exudate usually obscures the right psoas shadow.

The white-cell count is moderately raised in the early stages and the serum amylase may be elevated from coincident pancreatic damage or even from the retroperitoneal duodenal collection.

TREATMENT

It is imperative to repair the duodenal tear as quickly as possible, and once the diagnosis has been established or even suspected the patient should be prepared for surgery after any blood loss or fluid and electrolytic imbalance has been corrected. Naso-gastric suction by a Ryle or other tube is mandatory. Thorough exploration of the abdomen is necessary, remembering that multiple lesions may be present and that intraperitoneal signs of duodenal rupture may be few or absent. The commonest are: a variable amount of serosanguineous free fluid; haematoma formation in the retroperitoneum or mesentery of the transverse colon or small bowel, sometimes tinged by bile; crepitation in the retroperitoneum or collection of air bubbles on the serosal aspect of the colon; and fat necrosis of retroperitoneal tissues. Any other lesions in the abdomen should be first searched for and remedied, and then the second part of the duodenum "Kocherized" by incising the peritoneum along its lateral avascular border and turning the bowel medially. If the region of the ampulla is involved the common duct should be identified, as it may need to be reimplanted (Welch, 1951).

The local treatment of the perforation will be to close it, if at all possible, without narrowing the lumen grossly. If stricture seems likely from this procedure the following measures have been adopted: (1) complete division of the duodenum and an end-to-end anastomosis; (2) complete division of the duodenum, closure of both ends, and gastrojejunostomy; and (3) closure of the distal duodenal stump and duodenojejunostomy. Drainage of the retroperitoneal area through a stab wound in the flank is the next most important step, as the retroperitoneum is peculiarly liable to prolonged phlegmonous suppuration—even with this precaution. Parenteral fluids, gastric suction, and antibiotics are continued until intestinal function is firmly established. In the convalescent phase a barium-meal examination is advisable to exclude stricture formation at the site of repair.

Complications include peritonitis, paralytic ileus, retroperitoneal cellulitis, external duodenal fistula, local or subphrenic abscess, stenosis of duodenum or bile ducts, duodenocolic fistula, pulmonary collapse or infection, and wound infection and dehiscence.

CASE REPORT

A 19-year-old soldier was admitted to a British military hospital in Germany on September 28, 1955. That afternoon, whilst manœuvring lorries in an enclosed space, he had been crushed between the back of one and the radiator of another. He had immediately experienced severe pain in the left loin and left side of the abdomen, which had continued unabated. He had not vomited. When seen he was groaning in pain. The pulse was 88, temperature normal, and B.P. 110/80. Tenderness and guarding were present mainly over the left side of the abdomen, and a large haematoma filled the left loin. An *x*-ray film showed fractures of the transverse processes of L 1–4 on the left side. Rectal examination was negative and normal urine had been passed since the accident. Bowel sounds were absent. His symptoms were thought to be due to his spinal injuries, and 100 mg. of pethidine was given. Two hours later the pain was still severe and there were generalized guarding and release tenderness, with rigidity maximal on the left side. An *x*-ray film of the chest was taken to show the diaphragms for the presence of free gas under the right cupola. This was absent, but the presence on the wet film of free gas around the right kidney, giving a characteristic "pneumogram," was overlooked. This was the most important single finding, as the other signs were not at all indicative of a right-sided lesion. A tentative diagnosis of retroperitoneal rupture of the *left* side of the colon was made and preparations for laparotomy were instituted after gastric suction and intravenous saline were set up.

Operation.—Under general anaesthesia a left paramedian para-umbilical incision was made. A small amount of bloody free fluid was present, but the left side of the colon was normal. A large retroperitoneal haematoma was visible, and palpable, around the right kidney and infiltrating the mesocolon and small bowel mesentery. The most striking feature was the presence of numerous beaded bubbles of air trapped between the serosal and muscular coats of the right half of the transverse colon, and there was a crepitant collection of air around the right kidney. For better exposure a transverse extension was made across the right rectus above the umbilicus, converting the wound to a T shape. The small bowel was intact and no other lesion was seen, so the right colon was reflected medially by incising the parietal peritoneum on its lateral aspect. Bile mixed with the blood was found in the haematoma and only then did the true diagnosis come to mind. On reflecting the second part of the duodenum medially, the bile was seen to be coming from a tear at the junction of the second and third parts of the duodenum which involved two-thirds of its circumference. The margins of the tear were swollen and oedematous. A repair was effected at right angles to the bowel axis with two layers of catgut, the first embracing all coats and the second in Lembert fashion. Owing to the size of the tear and the oedema around it the resultant repair caused some misgivings concerning the adequacy of the duodenal lumen. However, no trouble occurred post-operatively. A large drain was led down to the area retroperitoneally via a stab incision in the right flank, and the abdomen was closed in layers.

Post-operative Progress.—Bowel function was finally established on the sixth day, when gastric suction and intravenous alimentation were discontinued. Progress was good until the 14th day, when he coughed up some blood and had signs of a right lower lobe collapse, no doubt due to a pulmonary embolus, though there was never any calf tenderness. Pulmonary signs rapidly abated, but pyrexia continued and large amounts of pus were intermittently discharged from the drainage track in the right loin. The pus grew *E. coli*, and a course of chlortetracycline, to which it was sensitive, was given. A month after operation a tender indurated mass could be felt in the right iliac fossa, extending up towards the right kidney. The drainage track was dilated, some pus evacuated, and a rubber drain reinserted. However, the mass grew larger, and it was obvious this residual abscess would have to be evacuated more directly. On the 42nd day a gridiron type of incision was made under general anaesthesia in the right iliac fossa, and, keeping extraperitoneal, a loculated phlegmonous mass was found on the posterior abdominal wall. The original track was dilated and some pus evacuated from the perinephric region and drainage instituted from either end of the gridiron incision.

In two days he was afebrile, though the drains discharged for a further three weeks, and he rapidly gained weight and strength. Ten weeks after operation a barium-meal examination showed no hold-up at the site of repair, which could barely be detected. Eleven weeks after operation he returned to his unit on light duties. His original T-shaped laparotomy wound had healed excellently and there was no sign of weakness in it. Fourteen months later he was very well and had no digestive or abdominal symptoms (postal communication).

J. A. HANLEY, M.Ch., F.R.C.S.,
Major, R.A.M.C., Surgical Specialist.

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Reviews

CHRONIC ILLNESS IN THE U.S.A.

Chronic Illness in the United States. Volume I—*Prevention of Chronic Illness.* By the Commission on Chronic Illness. (Pp. 338+xxii. 48s.) Cambridge, Mass.: Harvard University Press (for the Commonwealth Fund). London: Oxford University Press. 1957.

In June, 1949, a Commission on Chronic Illness was constituted in the State of Illinois "to study a complex nation-wide problem" in the United States. There were 46 members, about half of them doctors; 41 technical experts gave advice, staff associates were appointed, and special contributions were prepared and reviewed by various interested associations and societies. Literally hundreds of people shared in the work of the commission, and when it was dissolved in 1956 the Commonwealth Fund undertook the publication of their considered opinions and conclusions in four volumes, of which this is the first.

The book is in two parts; 100 pages are devoted to general problems. Primary prevention is defined as "averting the occurrence of disease," which is usually impossible unless we have some knowledge of the cause and can deal with it; secondary prevention is "halting the progression of a disease and preventing complications"—what is usually described in Britain as alleviation or treatment. There are chapters on screening tests and community planning, and four pages of conclusions and recommendations. Despite its distinguished provenance, this section of the book is diffuse and more than a little dull; the caution of many critics smothers individual inspiration, and the result is a medley of vague platitudinous exhortations to various interests to get together and do something. The dentists, however, are a distinguished exception; they at least give forthright advice that communities should adopt fluoridation of water supplies to prevent caries.

The second part of the book is better; it consists of summaries of information about 18 selected types of chronic disease, which are clearly written and informative; useful (but almost exclusively American) lists of references follow each summary. None of the information is new, and almost all of it is already available in textbooks. Nowhere is the problem of responsibility for the care of the chronic sick squarely faced. Is it the duty of society to shoulder the burden, or should it be left to the friends and relatives of the afflicted with such help as they can get from charitable or public services? "Decisions where to locate responsibility for community planning," it is stated, "will depend largely upon the fact that leadership is where you find it . . . and the list of possible candidates for the leadership is a long one." That is the considered but not very helpful judgment of the members of the commission. Nevertheless they are pleased with the result of their labours, which cost nearly 600,000 dollars; so confident were they of the impetus which their programme had given to "progress in chronic illness" that they were sure that their dissolution in 1956 would not affect the forces of unity they had set to work.

A. P. THOMSON.

CANADIAN MEDICAL SERVICES IN THE WAR

Official History of the Canadian Medical Services 1939–1945. Volume I—*Organization and Campaigns.* Edited by W. R. Feasby, B.A., M.D. (Pp. 568+xii; illustrated. $5.) Ottawa: Edmond Cloutier, C.M.G., A.O., D.S.P., Queen's Printer and Controller of Stationery. 1956.

Once when talking to a Canadian on the subject of Canada's war effort I was reminded, "Well, aside from all else, a man looks after his mother." In this large volume we have the story of how Canada's sons and daughters came to the assistance of the Motherland in World War II and how the medical services played their part in the defence of our way of life. This Canadian saga covers a wide range; it deals with the growth of the (to be) "Royal" Canadian Medical Corps and the formation and history of the offshoots from that central stem—the naval, air force, and nursing services. Then follows in considerable detail the part those services played in support of the fighting troops throughout the war. There is a good medical picture of the tragic epic of the Dieppe raid, and many a factual story of the gallant behaviour and fine professional work of the Canadian doctors, nurses, and auxiliaries in Italy, France, and far-off Hong Kong.

One finds that the Canadian character is well delineated. A Canadian takes nothing for granted. Like Kipling, he keeps six trusty working men who taught him all he knew; their names are What and Why and When and How and Where and Who. Once convinced that something new is sound, all his energies go into making it work. This is seen in the acceptance of the Hartgill Committee recommendations for the field medical units. Suspicious at first that some of the innovations were not all they were claimed to be, the Canadian medical services were the first really to try out the scheme; they made it work and work well. The Canadians were also the first to test out and put into practice a way of placing a round peg in a circular hole, and it was their idea which created the Pulheems system of personnel selection, which, modified, still seems the best way of sorting men into their correct category or, rather, giving a man a realistic label to indicate what he can be expected to do well in his own individual capacity.

The format of this history runs much to standard, and it has several interesting features. The maps are excellent; would all editors of such histories please note the method of inserting maps so that they can be "folded out"? It is a pleasure to find that the nursing and auxiliary services, to whom high and justifiable praise is given, are not overlooked in this story of the medical services. The editor has compressed a great deal into a comparatively small space; the text is clear and concise and gives a fine picture of the invaluable work performed by the medical and the sister professions from the Canadian angle in World War II.

J. C. A. DOWSE.

TREATMENT OF ASTHMA

Therapy of Bronchial Asthma. Proceedings of the International Round Table Friendship Meeting of Allergologists held at Utrecht, Holland, in 1955. Edited by Jhr. Dr. W. J. Quarles Van Ufford. (Pp. 354+xvi; illustrated. 50s.) Leyden: H. E. Stenfert Kroese N.V. 1957.

Experts from 18 nations met in Utrecht in 1955 to discuss the treatment of asthma. This book is a verbatim report of the papers read by various contributors, together with ensuing discussions. As might be expected, the views expressed are somewhat divergent and do not altogether give a harmonious and simple guide to the treatment of asthma. In the early chapters contributors convincingly state the case for the allergic basis of asthma and describe in detail the treatment of desensitization. Failure by this method is traced to a faulty technique in skin testing and to incorrect administration of the allergens. Nevertheless, carefully planned observations from Denmark made it clear that about a third of the patients with asthma improved just as well with a placebo as with specific treatment. This surely is a yardstick to be remembered when assessing any form of treatment for the disease. Unfortunately this fact is overlooked by many of the later contributors, who enthusiastically adhere to other forms of therapy. Apparently asthma can also be cured by living at high altitudes, thermal spas, psychotherapy, physiotherapy, hormones, antibiotics, surgery, and even by gold. The value of a book of this sort, however, is not in the answers it provides so much as in the ideas it provokes, and there is plenty of food for thought. An unusual and disturbing feature of the book is that on page 169 it suddenly becomes written in French for one chapter. However, there follows an excellent translation into English and there are no further lapses.

T. PARKINSON.

BUCKSTON BROWNE

Sir George Buckston Browne. By Jessie Dobson, B.A., M.Sc., and Sir Cecil Wakeley, Bt., K.B.E., C.B., LL.D., D.Sc., F.R.C.S., F.R.A.C.S., F.A.C.S. Foreword by Sir Harry Platt, LL.D., M.D., M.S., F.R.C.S., F.A.C.S. (Pp. 143 + viii; illustrated. 25s.) Edinburgh and London: E. and S. Livingstone Ltd. 1957.

The career of Sir George Buckston Browne was, and is likely to remain, unique. Without the possession of a higher surgical diploma, without the advantage of being on a hospital staff, without wealth or social influence to make his way easy, he deservedly achieved a distinguished position in the surgical profession, gained a large and influential practice, and incidentally amassed a large fortune, much of which he generously gave away to further the progress of surgery. It is true that he practised a rather narrow specialty, and one must agree with Sir Hugh Lett's statement that "never again will it be possible for anyone to have a practice of a similar character and size." Yet his was a great achievement.

Buckston Browne was born in Manchester in 1850, the son of a doctor who had strong religious convictions but little common sense. He said: "My father and I were the very opposite. We never had a thing or a thought in common." Matriculating from Amersham Hall (and having Augustine Birrell as a fellow-student), he decided to become a doctor and trained at University College Hospital, where as a houseman he impressed Sir Henry Thompson, who took him as his assistant. Thompson took three months' holiday every year, and that gave Browne his chance. He soon became as skilled as, or more skilful than, his master, and, after thirteen years, practised entirely independently. He worked early morning and late evening seven days a week, for thirty years took no holiday, did not employ a secretary but wrote all his letters in long-hand, and became the confidential surgical adviser of many of the leading men in business and politics. He was a great walker and a notable swimmer, and lived to the ripe age of 94 years.

All surgeons should read this book, both for its intrinsic interest and for the many useful lessons it teaches. It concludes with a quotation from Buckston Browne's notebook:

> Still pluck will win. Its average is sure.
> He wins the prize who will the most endure,
> Who faces issues, he who never shirks,
> Who waits and watches, and who always works.

ZACHARY COPE.

MEDICAL LABORATORY TECHNOLOGY

An Introduction to Medical Laboratory Technology. By F. J. Baker, F.I.M.L.T., F.I.S.T., F.R.M.S., R. E. Silverton, A.I.M.L.T., F.R.M.S., and Eveline D. Luckcock, A.I.M.L.T. Second edition. (Pp. 408+xiv; illustrated. 35s.) London: Butterworth and Co. (Publishers) Ltd. 1957.

The appearance of a second edition of this work three years after the first is an evident indication of its popularity. The book aims at covering completely the syllabus for the intermediate examination for the Institute of Medical Laboratory Technology, and it would certainly appear that any candidate who knows everything in the present volume should have no difficulty with this examination. The new edition is nearly 100 pages longer than the previous one, and contains extra sections on gastric analysis, culture media, and blood transfusion technique. A new departure is a section on elementary physiology, and, while the difficulties of covering this subject in 12 pages can be readily appreciated, this section is perhaps a little too incomplete to be of real value. It may, however, serve to stimulate the reader's interest and to encourage further reading.

The book is well produced and the sections are well written and arranged, although one might perhaps suggest reversing the order of the two parts of Chapter 9 ("Faeces and Gastric Analysis"). It can be confidently recommended for the purpose for which it was written, and the new edition seems likely to be at least as successful as the previous one.

N. F MACLAGAN.

OUTLINE OF HISTOLOGY

Human Histology: A Textbook in Outline Form. By Leslie Brainerd Arey, Ph.D., ScD., LL.D. (Pp. 337+ix. 45s. 6d.) Philadelphia and London: W. B. Saunders Company. 1957.

There are several distinctive features in this new textbook by the Emeritus Professor of Anatomy in the Northwestern University of Chicago. It has no illustrations, it has no sentence exceeding one line in length, it deliberately groups information in classes by progressive indenting of the subordinate matters, it proceeds by a series of dogmatic statements, it makes no call on the reason, it requires no thought but a good memory, it does not restrict itself to histology but expands both into gross morphology and also into physiology, but presents no evidence and offers no alternative views, still less the impression that they could exist. It is somewhat difficult to see to what type of mind it could appeal or how such a mind could function when diagnosing a case. The presentation of facts is clear-cut, but, being without evidence, this should be restricted in the main to those facts largely accepted without dispute.

A. ST. G. HUGGETT.

ELECTROCARDIOGRAPHY FOR BEGINNERS

An Introduction to Electrocardiography. By L. Schamroth, M.B., B.Ch.(Rand), M.R.C.P.E., F.R.F.P.S. (Pp. 60+xi: illustrated. 12s. 6d.) Oxford: Blackwell Scientific Publications. 1957.

This little book is very short, and that is an advantage when so many books on this subject are so large. To attempt such brevity is praiseworthy, but difficulties in expression may make understanding longer. The basic principles are illustrated solely by unipolar leads, and this is good. The effect of altered position of the heart is well done, but one misses some remark on the T waves. The diagrams of infarction show larger lesions of the right ventricle than are usually seen at necropsy. The explanation of the current of injury is rather unusual, but probably comes to the same as that commonly given. The explanation of bundle-branch block is rather limited. Throughout there are numerous clinical comments, so that this background is well expressed. The chapter on disorders of rhythm has very complex diagrams which do not always make things clearer. But despite some defects this little book does something to start the beginner to understand a subject that many writers make difficult and obscure.

TERENCE EAST

Volume 25 of the *Brompton Hospital Reports* contains reprints of 24 papers published in 1955 by members of the staffs of the Brompton Hospital, London Chest Hospital, and the Institute of Diseases of the Chest. This volume, which completes a quarter of a century of the *Reports*, appropriately contains author and subject indexes to all 25 volumes. It is published by Lloyd-Luke (Medical Books) Ltd., 49, Newman Street, London, W.1, price 15s.

The Doctor's Signature (Victor Gollancz Ltd. Price 13s. 6d.) is a first novel by Hamilton Johnston about general practice in an industrial town. Dr. Truscott—"shabby, lovable, and sexually misadventurous," as the blurb describes the hero—is a middle-aged Lucky Jim. Like Mr. Kingsley Amis, Mr. Johnston raises laughs by putting his characters into the most uncomfortable predicaments and then rescuing them before they are overtaken by final disaster. General practice is no more than a suitable background for the author's observations on the lives led by business and professional people in a narrow provincial environment. The melodramatic central theme, with a mysterious millionaire hatching shady financial plots, seems hardly necessary, and Dr. Truscott is too plainly a puppet in this tycoon's hands. This is strange, because the doctor is almost too good at his job: he can read radiographs of the skull at a glance, instantly knows what to prescribe for a man with a brain tumour who complains that he smells burning paper before having a fit, and has no difficulty in identifying a sugar-coated pill by cracking it open and tasting the contents. Apart from these trivialities, however, the book is easy reading, has some shrewd things to say about doctors and their ways, and is, in places, very funny indeed.

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HORMONE THERAPY FOR ATHEROSCLEROSIS

It will be a major advance if some therapy is found to restrict the development of atheroma, whether by reducing levels of cholesterol in the blood, combating any thrombotic tendency, or preventing destruction of the arterial wall. In certain species it has been clearly established that the degree and extent of fatty atheromatous lesions are directly proportional to the height and duration of experimentally induced hypercholesterolaemia, and that these lesions subsequently regress with reduction in the level of cholesterol. Since in man hypercholesterolaemia is positively correlated with the clinical manifestations of coronary atheroma,[1] a working hypothesis is often assumed that reduction of hypercholesterolaemia might lead to less deposition of cholesterol on and under the arterial intima. This hypothesis cannot yet be confirmed or refuted, since all attempts to reduce hypercholesterolaemia are still at an early experimental stage. Alteration in diet by restricting the intake of fat or the addition of polyunsaturated fatty acids, and treatment by means of certain hormones, are at present being studied as methods of lowering permanently the blood levels of cholesterol.

The effect of various hormones on the circulating cholesterol and lipoproteins has recently been reviewed.[2 3] Two main groups of them—the thyroid and oestrogenic hormones—will reduce the level of cholesterol in the blood. In theory, thyroxine is unsuitable for lowering hypercholesterolaemia in patients in whom the myocardial blood supply and oxygenation are impaired by coronary atherosclerosis, because any resultant increase in metabolic demand could lead to myocardial ischaemia and produce symptoms. However, J. Lerman and R. Pitt-Rivers[4] have shown that in myxoedema small doses of triiodothyroacetic acid (triac) lowered the plasma cholesterol without raising the basal metabolic rate. Moreover, a similar dissociation of action has been observed with triac[5] and triiodothyronine[2] in euthyroid, hypercholesterolaemic patients with coronary disease. Unfortunately, M. F. Oliver and G. S. Boyd[6] found that depression of the level of plasma cholesterol could not be long maintained without constant increases in the dose of triac, leading eventually to a rise of the basal metabolic rate. Some of their patients, and those of I. R. Mackay and colleagues,[7] developed angina even when the B.M.R. remained unaltered. Experimentally, triac and triiodothyronine selectively increase the oxygen consumption of certain tissues,[8] particularly myocardium, and thus this development of angina could be explained by an increase in the oxygen requirements of the myocardium which was not reflected by a change in the B.M.R.[9] Any analogue which will depress the plasma cholesterol over long periods without increasing the oxygen requirements of the myocardium may have considerable therapeutic importance.

Various workers[10 11] have shown that oestrogens lower hypercholesterolaemia in patients with atherosclerosis, and that this effect can be maintained over long periods. Unfortunately, it has not yet been possible to reduce hypercholesterolaemia with oestrogens without also producing feminization. Most men experience gynaecomastia and loss or depression of libido, and, though these feminizing effects can be tolerated, they obviously limit the general use of oestrogens as a therapy for lowering the level of plasma cholesterol. Attempts to modify the feminizing effects by the simultaneous administration of androgens have resulted in loss of the cholesterol-depressant effect without any significant change in feminization.[10 11] It is possible that weakly oestrogenic oestrogens might lower hypercholesterolaemia without feminization, but, though progress has recently been made in this direction,[12] separation of these actions has not yet been achieved. If such a "non-oestrogenic" analogue can be found, it may have wide therapeutic potentialities in view of the experimental evidence that oestrogens can prevent the development of atherosclerosis.

Thus there is no satisfactory hormonal treatment of hypercholesterolaemia at present. Thyroid and oestrogen analogues may prove valuable, but much work is required before they can be used outside the field of clinical research. Ultimately any therapeutic regime will have to be judged by its influence on morbidity and mortality from atherosclerosis rather than by its ability to lower hypercholesterolaemia.

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PAYING FOR THE HEALTH SERVICE

The Health Service is paid for out of taxes, rates, charges to patients, and the Health Service portion of the weekly National Insurance contributions. The last, which is included in the weekly stamp, is inherited from the old National Health Insurance scheme. There are, in addition, other receipts that offset the gross total of the Service's expenditure—for instance, the excess of superannuation contributions over payments. But the people of Britain, as a whole, meet the bulk of the Service's cost in one or more of these four ways. It is as taxpayers they pay most and as ratepayers least. In 1957–8 the estimated amounts are roughly: taxes £545m., insurance contributions £63m., patients' payments £34m., and rates £29m.

A year ago the Government decided that the proportion of the cost borne by the taxpayer was high enough, and it was consequently faced with the alternative of refusing to allow the gross total cost of the Service to rise (which in a time of rising prices would have been tantamount to a cut in the Service's facilities) or of increasing the charges to patients or of increasing the part of the National Insurance contribution that goes towards the cost of the Health Service. (The ratepayers' obligation is limited by the amount that the local authorities choose to spend.) The Government decided that the most painless way out of the dilemma was to increase the insurance contribution. It accordingly introduced a Bill that doubled the total amount to be paid from the National Insurance Fund towards the cost of the Health Service from just over £40m. to £80m. (in a full year), and the new contribution came into force last September. This meant for the individual that, out of his total National Insurance contribution, a man paid 1s. 4½d. a week towards the Health Service and his employer 3½d. Previously he had been paying 8½d. and his employer 1½d.

Now the cost of the Health Service is rising again. Last year's increase in the insurance contribution was to meet a prospective gross total of expenditure on the Health Service of nearly £690m. Next year, 1958–9, the gross total is expected to be £740m. So the Government has been faced with the same dilemma, and has again chosen to meet the increase by higher insurance contributions rather than by taxes or patients' payments. The insured man's weekly contribution to the Health Service included in his stamp will go up to 1s. 10½d. and his employer's to 5½d., with smaller increases for women and juveniles. This will bring in an additional £24m. in 1958–9 (the new contribution will come into force in July) and £32m. in a full year, and the actual effect on the estimates is to reduce the amount to be borne by the taxpayer from £545m. in the current financial year (after taking supplementary estimates into account) to £530m.

It is clearly better that the healthy should pay more towards the cost than the sick person, once it is accepted that no more can be laid on the taxpayer's shoulders. And, as the Chancellor of the Exchequer explained last week, the future proceeds of the contribution, together with the charges paid by patients, will still amount to just less than one-fifth of the total gross cost of the Health Service.[1] This was the proportion that the insurance contribution alone was intended to meet when the Service was planned, but because of the huge rise in money costs it was actually only about one-eleventh of the total of £450m. in 1949–50. But, if costs go on rising, can the Government go on putting more on the insurance stamp? Being a flat sum, it falls more heavily on the lower-paid workers—though they pay relatively less in direct taxation towards the Service's cost. Perhaps this is only an interim measure, which will be superseded when the Government's new plans for old-age pensions are announced. If insurance contributions for pensions are to vary with earnings, as is now being discussed in political circles, the total cost of the weekly stamp will not seem so heavy to people with smaller incomes as it does now.

[1] *Brit. med. J.*, 1958, **1**, 469.

DISEASE EDUCATION BY THE B.B.C.

The B.B.C.'s programme *Your Life in Their Hands* was the subject of a debate by the Council of the B.M.A. last week. A full report of this appears in this week's *Supplement*. As a result of the debate the Council passed a resolution referring to the anxiety and distress caused to some members of the public as well as to doctors as a result of this programme, and expressing its firm opinion "that the emphasis in television and sound broadcasting programmes of a medical nature should be on health rather than on the sensational presentation of disease." The liveliest interest is being displayed by the press in the subject and in the opposition to the series in the editorial columns of this *Journal*. Those doctors who sincerely believe that televising details of disease would benefit the public presumably don't mind if some individuals here and there are shocked or upset or made anxious about this, so long as the alleged benefit is obtained for the majority. If this be the case, it is an attitude which is quite contrary to that traditionally held by the individual doctor looking

after the individual patient. The first letter in our correspondence columns this week, from a general practitioner, points the dilemma: as a result of a television programme the patient guessed correctly that he was suffering from cancer, a diagnosis which in the interest of the patient the practitioner had not disclosed to him. Another general practitioner has written to the B.M.A. to say that as a result of the televising of the cancer programme in the *Your Life in Their Hands* series patients attending his surgery have become jittery, and one patient with a benign swelling is now firmly convinced that it is cancerous. As the result of an apparently innocuous remark made in this programme, the confidence of a patient with cancer in the likelihood of cure was violently shattered; this was from another practice. A speaker in the Council debate referred to the worry experienced by a hospital sister lest the patients in her ward, having deep *x*-ray therapy, should guess what it was for by seeing the telecast or hearing it discussed. This and other damage has been done and cannot now be undone. These incidents do not surprise us in the least, and we are sure that they were unforeseen by those planning this programme and taking part in it. The treatment of disease is first and foremost a highly individual matter between the doctor and the patient, part and parcel of what is meant when we talk about the doctor–patient relationship. Because the hospitals are now owned by the State, and therefore the owner, the Ministry of Health, can give a national broadcasting corporation permission to enter the public wards, does not justify the intervention of the television camera in the doctor–patient relationship, even though in the particular circumstances the two sides agree to it. For this reason. What they are exhibiting on the television screens all over the country is not solely and simply Mrs. X's heart operation, or Mr. Y's cirrhotic liver. They are by this means intervening in the doctor patient relationship of other practising doctors. They are raising doubts and fears in the minds of their colleagues' patients, and already with one or two distressing, if not disastrous, results, which we consider it is impossible to justify on the highly questionable grounds that the majority will benefit from knowing something about disease.

The second part of the Council's resolution surely points the way to an intelligent and constructive approach to the popularization of medicine. An endless number of topics of preventive medicine in the wider sense of the term lend themselves to the kind of treatment in which the two mass media are so expert. If the B.B.C. were once again to bend its efforts in this direction they would be in line with all the efforts made since the end of the war to place the emphasis on health rather than on disease. That is why industrial medicine is now usually described as occupational health. Diseases of childhood, or even paediatrics, are terms which have given way to child health and child care. The organized provision of a medical service in this country was described by the Government as a National *Health* Service. But what was the point of giving the public on Tuesday night a clinical demonstration of a case of mitral stenosis, followed by cardiac catheterization "on a colleague," and a seven-minute film of mitral valvotomy? It was suitable enough for medical students at one phase of their education, but not, surely, for the uninstructed. Let us hope that the B.B.C.'s present preoccupation with disease is a passing phase and not part of a policy that, if continued, will make Britons disease-conscious people.

ACUTE RESPIRATORY DISEASE IN BABIES

Recently an acute respiratory disease of babies has been reported[1]; it is of uncertain aetiology and had a particularly high incidence in London and Birmingham. Most of the infants are under 12 months of age and many under 3 months. The disease attacks without predilection for social class or nutritional status. In many instances there is a history of coryza in an adult or older child in the family, and the baby's illness starts two or three days later as a simple infection of the upper respiratory tract, perhaps associated with a paroxysmal cough, mild conjunctivitis, and some vomiting—rather like pertussis. Then a few days later—or it may be within 24 hours—a dramatic and alarming deterioration develops, characterized by acute respiratory distress, pallor, and collapse, but cyanosis is not a feature. On admission to hospital this clinical picture is associated with signs of circulatory failure, restlessness, an acute diffuse and widespread bronchiolitis, sometimes of an asthmatic type, but signs of frank consolidation are exceptional. The pharynx and throat are congested and there is some non-purulent nasal discharge. Radiological examination may show little change or there may be a little patchy emphysema, small scattered areas of consolidation, or occasionally collapse of part of a lung.

While a virus is suspected as the aetiological agent, this has not yet been established. Studies to date seem to indicate that in most cases so far examined viruses of the adenovirus or Asian influenza type are not responsible. But there is no doubt that the staphylococcus plays an important part, probably as a secondary invader, though further investigations are needed to decide this with certainty.

In treatment, oxygen is vitally important in about a quarter of the cases, and in the severe ones high concentrations of oxygen for short periods are particularly beneficial. Antibacterial therapy is indicated mainly if not specifically to combat secondary or additional

[1] *Brit. med. J.*, 1958, **1**, 410.

infection, and as the staphylococcus is the particularly dangerous and threatening organism it is unwise to depend on penicillin only. A combination of penicillin and streptomycin or alternatively tetracycline would appear to be the drugs of choice in the present state of knowledge. In a few cases intravenous hydrocortisone has been life-saving.

The duration of the acute manifestations of the disease can be measured in days; some babies are convalescent within 48 to 72 hours, and only rarely does the illness run into the second week, in particular those desperately ill on admission. Complications that have been encountered include extensive pulmonary collapse, frank consolidation affecting one lobe or more of the lung, and in a few cases pyopneumothorax; these are clearing up satisfactorily. Despite the critical clinical condition of many of these babies on admission to hospital, the mortality rate remains low, and may be estimated at about 2–3%.

ANTIBIOTICS IN HEPATIC COMA

The syndrome of hepatic coma and precoma in patients with liver disease has been related to the absorption of toxic nitrogenous substances from the intestine.[1-3] They may be derived from dietary protein or amino-acids such as methionine. Blood oozing from gastro-oesophageal varices also provides a rich protein meal. It is probable that these intestinal products include ammonium and amines and that they are metabolized by the normal liver. But, in the presence of liver-cell dysfunction or large portal collateral vessels by-passing the liver, these noxious substances pass directly from the intestine to the brain, producing degrees of encephalopathy which range from drowsiness and disorientation to deep unconsciousness. This so-called portal–systemic encephalopathy may be sudden and fulminant or it may be insidious and intermittent. To a large extent this depends on the state of the liver and the extent of the portal collateral circulation. Hepatic necrosis due to fulminant virus hepatitis may lead to acute and deep coma, which is often irreversible and fatal. On the other hand, an extensive portal collateral circulation even in the presence of well-compensated cirrhosis may be sufficient to promote intermittent or chronic low-grade metabolic poisoning of the brain over months or years.[4] Since it is insidious, this chronic intermittent variety of hepatic coma is more likely to be overlooked than its acute, fulminant counterpart, though the latter may also present initial difficulties if its abrupt onset precedes jaundice. In assessing hepatic precoma, or for that matter any suspected liver disease, it is therefore important to judge the degree of liver-cell dysfunction and also the extent of the portal collateral circulation.

To these two factors must be added a third, which appears to be operative in all forms of hepatic coma. The normal small intestine is virtually sterile, whereas that of the cirrhotic patient bears an abundant flora of organisms, particularly coliforms.[5] These intestinal organisms are known to break down protein and methionine, with the liberation of ammonia and amines,[6,7] thus increasing the toxic load conveyed to the brain through the diseased liver or via the portal collateral circulation. Elimination of this bacterial factor has indeed provided gratifying results in the control of hepatic coma. The antibiotic chosen must be given by mouth, for it is to have a local intestinal effect. It should have a wide antibacterial range to deal with the mixed flora of the intestinal tract. Finally, it should preferably be bactericidal and of low toxicity. There are now many chemotherapeutic agents which come near to satisfying these requirements, but the problem of bacterial resistance with their continued use will always provide indications for the clinical trials of any others as they become available. It is even possible that a combination of intestinal antibotics may prove still more efficacious.

Early trials confirmed the value of combining chlortetracycline with restriction of dietary protein.[8] Thirty-nine of 66 patients in one series recovered; this was particularly notable since 21 of the survivors had been in deep hepatic coma.[9] More recently, neomycin has been preferred.[10-12] Its continued long-term use has proved less troublesome to the patient than the tetracyclines, though its present price is unfortunately a discouraging factor. Oral neomycin, in doses of 4 to 6 g. daily, has been shown to produce an early fall in the blood-ammonium levels.[12] In the ensuing weeks the fall does not appear to be sustained despite continued clinical improvement.

Further work on bacterial metabolism will make it easier to choose the method of intestinal chemotherapy, but this will remain only one factor in the management of hepatic coma. Laxatives or enemas also play their part, a fact which recalls older theories of intestinal intoxication in the causation of disease. Oral antibiotics, purgation, restriction of dietary protein, avoidance of narcotics, judicious intravenous infusions—all of these have a role in the prevention of impending coma, in survival from deep coma, or in converting an invalid with the chronic syndrome into a happier person.

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[11] —— —— *ibid.*, 1957, **256**, 1030.
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NATIONAL INQUIRY INTO PERINATAL MORTALITY

On March 1 a nation-wide inquiry begins in England, Wales, and Scotland into the causes of stillbirths and the deaths of infants aged up to 28 days. The reason why deaths in this group have been chosen for special inquiry is that, despite advances of clinical medicine

and public health, they have proved to be more difficult to prevent than have deaths at later ages in infancy and childhood.

The stillbirth rate in England and Wales has not changed much in the last ten years (though it has distinctly improved in Scotland, where the rate was higher), while infant mortality, though still falling, shows least improvement in the weeks nearest to birth. To investigate the reasons for this the National Birthday Trust has set up a Perinatal Mortality Survey under the directorship of Dr. Neville Butler, with a steering committee that includes representatives of all the main bodies concerned with the maternity services, including the B.M.A. Midwives will complete, under clinical direction, a questionary on every stillbirth and baby that dies within 28 days of birth in England, Wales, and Scotland throughout March, April, and May. They will also complete forms for all live-born babies born during March 3–9; these will serve as controls. The completion of questionaries on neonatal deaths on which the midwife is not in attendance may devolve upon health visitors or staffs of premature units of children's wards. Pilot surveys in Nottingham and south-west England have shown that information can be obtained satisfactorily in these ways and that parents are willing to co-operate. The inquiry will concentrate mainly on administrative and social matters, but some clinical information will also be gathered under the direction of general practitioners, paediatricians, and obstetricians, while pathologists will carry out necropsies to obtain precise data on the cause of death. It may then be possible to draw useful conclusions from the large mass of information obtained.

Recognition that some of the causes of stillbirth are the same as some of the causes of death soon after birth has led to the concept of "perinatal mortality" being developed.[1] Unfortunately conflicting usage has made it an ambiguous term. In what is probably its usual sense it covers stillbirths and infant deaths in the first week after birth, but some authors have attached the same meaning to it as the National Birthday Trust has—namely, stillbirths and infant deaths in the first four weeks after birth. To avoid confusion some agreement on a definition would seem to be desirable. Efforts to reduce the frequencies of stillbirths and deaths in early infancy have several aspects. First and most important has been the improved treatment of those conditions known to predispose to them, one example of which has been the increased foetal salvage rate after expectant treatment of placenta praevia. Secondly, a close liaison has grown up between obstetricians and paediatricians in the day-to-day management, with a growing concept of "antenatal paediatrics," while in many units regular conferences are held on perinatal deaths and the cause of death is determined with the help of a pathologist. Thirdly, many have felt that perinatal mortality may decline if better administrative facilities can be provided in what is already an overworked maternity service, and the recommendations of the Cranbrook Committee, which is reviewing the maternity service, are awaited with interest. Lastly, many clinical, pathological, and social investigations are being carried out. This new one, organized by the National Birthday Trust, should throw much light on problems that have so far been somewhat obdurate.

[1] *Brit. med. J.*, 1957, **1**, 216.

LOW BACK PAIN

Pain in the lower part of the back is one of the commonest symptoms encountered in medical practice. It is also one that needs thorough investigation, for it may be the presenting symptom of a serious organic disorder; consequently only methodical history-taking and physical examination are likely to reveal other features pointing to the true state of affairs. Moreover, radiographs of the lumbar spine and pelvis occasionally remain consistently normal when the backache is due to secondary malignant deposits, while the appearance of neurological signs may be delayed for many months despite the presence of an intraspinal neoplasm. These are but two reasons why a short physical and *x*-ray examination is not alone sufficient to guard against the possibility of making a serious error of diagnosis. Every case has to be considered on its merits and reviewed as often as seems necessary.

Among the more important organic causes of backache[1 2] are fractures of the vertebral bodies and their various processes; secondary neoplastic deposits; osteomyelitis and tuberculous caries; ankylosing spondylitis; Paget's disease; myelomatosis; and osteoporosis, whatever the cause. Fortunately the majority of patients complaining of low back pain are suffering not from a serious disease but from some form of mechanical strain or derangement of a lumbar joint, often accompanied by ligamentous or muscular damage. These conditions can lead to much discomfort and invalidism, but, largely because they are not fatal diseases, little is known of their pathology. Even so, during a discussion on low back pain held at the 1957 Annual Scientific Meeting of the British Medical Association[3] specialists working in different fields exhibited a remarkable identity of view in their fundamental approach to the subject. Doctors may well disagree over terminology, but will always applaud any approach that is carefully tested and controlled. However convenient they may be, such diagnostic tags as "lumbago," "low back strain," "lumbosacral strain," "sacro-iliac strain," or "postural backache" are best not used for purposes of technical record unless accompanied by an accurate definition of what the label means to the user in terms of clinical, radiological, and pathological findings. Only in these circumstances is an observer able to assess what his results mean when related to those obtained by someone else. It seems unlikely that general agreement can be reached on terminology until

[1] Davies, D. V., *Practitioner*, 1957, **179**, 123.
[2] Cooke, A. M., ibid., 1957, **179**, 129.
[3] *Brit. med. J.*, 1957, **2**, 230.
[4] Morgan, F. P., and King, T., *J. Bone Jt Surg.*, 1957, **39B**, 6.
[5] Schmorl, G., and Junghanns, H., *Die Gesunde und Kranke Wirbelsäule im Röntgenbild und Klinik*; Leipzig, 1932.

incontrovertible evidence is produced which will link easily recognized clinical and radiological syndromes with clear-cut pathological changes.

Recent work by F. P. Morgan and T. King[4] fills some gaps in our knowledge. The condition which they now term primary instability of lumbar vertebrae was originally described in 1932 by G. Schmorl and H. Junghanns[5] as "pseudo-spondylolisthesis," and by definition excludes instability secondary to old trauma, to spondylolisthesis, and to rupture of the nucleus pulposus into the spinal canal. Morgan and King carefully described the pathology of the associated traumatic and degenerative changes found in the intervertebral disk, together with the radiological techniques and criteria required for the diagnosis of instability. The mechanical disorder is an antero-posterior vertebral instability, allowing a glide of 0.3–1.7 cm. between the extremes of spinal flexion and extension. The basic lesion which allows this movement to occur is an incomplete posterior radial tear of the annulus fibrosus, usually between the fourth and fifth lumbar vertebrae, while in the upper lumbar spine there may be concentric fissures between the anterior lamellae of the annulus. According to these authors the characteristic features of the condition are low back pain associated with deep pain referred to the thighs, few or no neurological signs, and radiological evidence of antero-posterior vertebral instability. The disorder appears most commonly in men aged 20–40 and may give rise to chronic pain interspersed with episodes of acute pain, which is usually unaffected by coughing and sneezing. The neurological signs found in cases of nuclear prolapse are absent, and the test of raising the straight leg is usually unimpaired. Radiological evidence of instability is most commonly observed at the level of the fourth and fifth lumbar vertebrae and is rare at the lumbo-sacral junction.

Recognition of this type of lesion is likely to be of practical importance only if effective treatment is available, and then only if instability occurs sufficiently frequently unassociated with other manifestations of degeneration in the lumbar spine. The disorder was in fact observed by Morgan and King in 28.6% of 500 consecutive cases of low back pain. Most patients with vertebral instability were relieved by rest and a spinal support, and worsened by manipulation, though the manipulative method employed is not described. Those who suffered from intractable pain and had associated neurological changes required spinal fusion.

Owing to the nature of their symptoms, patients with primary intervertebral instability are apt to find their way to hospital in due course. Most of the sufferers from low back pain who visit their doctor will require only advice on the avoidance of unnecessary spinal flexion strains, and reassurance that they are not suffering from arthritis or a "slipped disk," since these terms are apt to conjure up visions of crippledom. Some patients require a short period of rest. Aspirin, liniments, and various forms of heat are time-honoured aids to recovery, and manipulation also has many advocates. A corset which effectively limits flexion of the lumbar spine may prove helpful in preventing a recurrence of symptoms. Nevertheless, when attempting to assess the results of treatment, it is worth remembering that, if given a reasonable chance, the great majority of patients with these disorders recover spontaneously.

ADOPTION

The new Children Bill now before Parliament amends the Adoption Act of 1950, and in so doing fulfils most of the recommendations of the Hurst Committee.[1] Doctors will welcome the clause which provides that the court, in determining whether an adoption order is in the best interests of the child, shall have regard to the health of the prospective adopters. The Government does not propose to prohibit third-party placings. The B.M.A. in its memorandum of evidence to the Hurst Committee said that there was great personal value in the best type of third-party placing and that it would wish this method to be preserved; but more safeguards against the risk of hasty uninformed placings need to be introduced. The well-being of the children concerned will generally be safeguarded by the application of the new provisions on child protection which form the first part of the Bill. The period of notice which must be given by the third party has been increased from seven to fourteen days, and this will give more time for investigation and tend to limit the risks of failure in this type of placing.

There has been much speculation whether the Bill would enable an adopted child to discover the facts of his parentage without an order from the court. The British Medical Association felt that there were advantages in providing means whereby the adopted child could satisfy his natural curiosity or protect his legal rights in respect of inheritance or title. The Government's decision not to make this provision is noteworthy in view of existing Scottish legislation which allows adopted children to obtain this knowledge at the age of 17. It is true that some witnesess from Scotland giving evidence before the Hurst Committee recommended that the age should be raised to 21 years, but, in general, the provision has been found entirely acceptable.

The three months' probationary period before an adoption order can be made, during which the child must live with the prospective adopters, will in future not start before the child is 6 weeks old. Even now the mother may not consent to the adoption before the child is 6 weeks old, but the probationary period at present counts from the actual date of placement with the prospective adopters; this may take place immediately after birth. The application of the probationary period to prospective adopters resident abroad may minimize the risk inherent in the provision which allows foreigners to come to this country in order to adopt a child. Possibly by this means homes may be found for coloured children, for whom there are far too few adopters in Britain. This proposal may well arouse much controversy, but it can perhaps be interpreted as evidence that the Government in the same way as the Hurst Committee is more concerned with the welfare of the child than with the satisfaction of the adopter.

[1] Report of the Departmental Committee on the Adoption of Children, 1954. H.M.S.O., London. See annotation in *Brit. med. J.*, 1955, 1, 276.

"STALINON": A THERAPEUTIC DISASTER

In a Paris court last December a French pharmacist, the inventor and vendor of a remedy against boils called "stalinon," was sentenced to two years' imprisonment and fined 1 million francs (about £850). Stalinon, it was alleged, had killed 102 people and left at least 100 others permanently affected. Damages of 643 million francs (£514,000) were awarded to the victims and their families. They had been poisoned in 1954. Our distinguished French contemporary "La Semaine des Hôpitaux" has devoted the whole of its latest therapy supplement† to an extended account (177 pages) of the stalinon trial. We are indebted to a medical correspondent in Paris for the following note on some of the toxicological and administrative implications of the case.*

The Trial

Stalinon was marketed as an oral preparation for the treatment of staphylococcal infections. It was dispensed in capsules, each containing 15 mg. of diiododiethyl tin and 100 mg. of isolinoleic acid esters (called "vitamin F"). A total of 400,000 capsules were made, but the cases of poisoning were accounted for by only 7% of these. A number of people took the capsules without suffering any untoward effect. In those who were poisoned cerebral oedema was found at necropsy or during exploratory operations. Headache was the first symptom, usually starting on about the fourth day after ingestion. It was extremely severe, and was often accompanied by repeated vomiting (and its consequences), disordered equilibrium, and retention of urine. Diplopia and pseudo-appendicular colic also occurred, though less often. Temperatures were normal or low. In the severe cases there was clouding of consciousness proceeding to coma, and in some there was residual paraplegia.

After a lengthy trial the pharmacist responsible for stalinon was given a maximum sentence—two years' imprisonment without remission, and a fine—because the required safety tests had not been carried out during its production. The technician who made the capsules was also charged, but he died before the trial began. He had in effect contravened the pharmaceutical regulations which require that the manufacture of drugs should be under the direct supervision of a graduate. Another assistant was fined.

The reason for these sentences was the fact established during the case that the clinical trial of stalinon, on which depended the Government sanction to market it, was carried out on capsules supposed to contain 50 mg. of diiododiethyl tin but which in fact, owing to a dispensing error, contained only 3 mg. The stalinon sold to the public therefore contained five times the amount of active material as was in the sample instead of a third as much.

From the legal point of view the stalinon case is now closed. The victims will be compensated, although the damages are so heavy that it is said that the insurance company specializing in the coverage of pharmaceutical firms which insured the makers of stalinon will find itself in financial difficulties. There remain, however, two outstanding questions, one medical and the other administrative.

Toxicological Investigations

Medically, what happened is still not quite clear: in particular, why there were no cases of poisoning for six or seven months. The trial naturally led to some interesting research. A Dutch chemist, Mr. Van der Kerk, showed that it was possible to prepare a pure diiodoethyl tin[1] which seemed less toxic than stalinon. A French pharmacologist, Professor F. Caujolle, showed[2 3] that organic tin salts had a delayed effect which made classical toxicity tests based on Trevan's method quite useless and needed for its detection prolonged observation of animals. The court's expert witness, Dr. Lebreton, failed repeatedly to produce toxic effects in animals (mice, rabbits, monkeys) with doses which did so in man. In monkeys—the most sensitive animal used—toxic symptoms were produced only with doses 3–10 times greater than those which had proved dangerous to man. Man therefore seems more sensitive to stalinon than animals.

Professor G.-M. Tréfouel and Dr. J. Matti, two chemists from the Pasteur Institute, explained the poisoning by showing that originally the capsules contained monobromodiethyl tin and monoiododiethyl tin but no diiodo derivative, and that the capsules would have been toxic only after the makers succeeded in really producing a diiodo compound. However, in animals the toxic effects of the monoiodo and the diiodo derivatives are identical. There was also some speculation on whether a toxic substance might have resulted from contact with oxidation products of isolinoleic acid. Finally, another unproved theory was that a triiodoethyl derivative might have been produced, for recently British workers have reported[4] oedema of the central nervous system in rats given such compounds. Their work, however, is too recent to have been confirmed. Thus, as in so many therapeutic disasters, some doubt remains about the exact explanation.

Control of New Pharmaceuticals

Finally, there is the administrative side. Can the premarketing testing of proprietary products in France be improved? It is easy enough to say that such tests are inadequate and always will be, but in France the testing procedures are considered very strict, and during the court case they were criticized only by those who wanted them relaxed. The French system makes the manufacturer wholly responsible for his product, though its sale is dependent on the approval of an expert scientific committee. This committee, which works in complete secrecy, examines the manufacturer's evidence and then advises the Ministry of Health. The evidence for a new product usually includes detailed reports of both the preliminary pharmacological studies and clinical trials directed by an expert. Nevertheless, this system did not prevent the stalinon case, since everyone was misled by the initial error. There was, too, the hitherto unappreciated factor of the delayed toxicity of tin, which became evident only after the disaster. And, furthermore, there was little available experience of the use of organic tin compounds; in fact, the only organic tin derivative known therapeutically was methyl stannic iodide, used in Britain under the name of "staniform" as an external application for staphylococcal infections. This product is no longer available commercially.

Perhaps I may draw three conclusions from this case. If the makers of stalinon had applied proper controls to their product, while they might have made no sensational discoveries, they would at least have abandoned their plans for putting it on the market. They would have found it was neither stable nor a uniform product and that it did not come up to the standard expected. Secondly, the case emphasizes the wisdom of the following comment in a recent W.H.O. Technical Report[5]:

> "This [the examination of pharmaceutical preparations] is a very difficult problem involving precise knowledge of many thousands of compounds. This large number of substances makes it almost impossible for any organization to be familiar with the whole subject. National pharmacopoeias usually describe a number of basic drugs. However, the preparation of a pharmacopoeia is a difficult task. . . . It is not possible to make available to control laboratories all the necessary information for the examination of the growing numbers of pharmaceutical preparations."

Lastly, this disaster in France shows how necessary is international scientific co-operation in such problems. As a result of the collaboration of Dutch chemists, French pharmacologists, and British toxicologists, we have added to our knowledge of the toxic properties of organic tin compounds.

H. P.

*_The Times_, December 20, 1957.
†_Semaine Thérapeutique_, 1958, **34**, No. 1.

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Correspondence

Disease Education by the B.B.C.

SIR,—This morning, when visiting a patient who was previously unaware of his condition, I was greeted with the query, "Doctor, have I got cancer of the lung?" On asking why he thought he might have cancer of the lung, the patient informed me that his treatment had been identical with that shown in a recent television programme dealing with that condition. Surely this is a very important point in considering the advisability of medical broadcasts.—I am, etc.,

London, S.E.18. JOSEPH ARMSTRONG.

SIR,—I was the lay journalist who "hovered on the verge of syncope, and one, it appears, not successfully" (*Journal*, February 15, p. 389).

As early as last November I was arranging with some national groups such as the National Association of Townswomen Guilds for group discussion to take place on this series, "Your Life in Their Hands," and my fear for the subject's reception has grown since that date.

I stated at the B.B.C. press conference at which the film cutting was shown that "you [medical people present] are living in a rarefied atmosphere if you think that the general viewing public are going to accept this series at its face value in the terms understood only by the medical practitioner." My point is this: from considerable experience of group listening and group viewing of both films and television I am only too aware that *at all times* most of us take in only a small percentage of what is before us *even when we are very interested in the subject matter*. Both films and T.V. are viewed *en masse* by disinterested and in the main ignorant people. (Viewing figures comparing I.T.A. and B.B.C. television programmes will, I think, amply prove this last contention.)

This large and uninstructed public is now to be treated to 13 programmes of a highly technical content. This does not matter where the subject matter has no relationship between technicalities and emotion (such as in pure science) built into it. But in the case of medicine the story is different. Whether consulting-rooms will be full of unbalanced viewers each sure that she has the previous night's ailment is comparatively immaterial. What does matter is that you cannot take the lid off something like medicine and make it suddenly understood by a few television programmes. Emotion plus inattentive viewing plus ignorance will defeat the avowed plan of the series—"to show that regional hospitals can do as well as the big London hospitals"; will undermine confidence, not increase it; and will in the long run increase the already well-planted fears of hospitalization, already existing, in the minds of such types as lay journalists like myself, who in cold blood cannot even "take it" as film in a preview theatre.—I am, etc.,

London, W.C.1. W. G. STITT-DIBDEN,
Editor, *Group View*.

SIR,—I was amazed at the outburst of righteous indignation by a certain section of the profession about television programmes which are appearing under the title of "Your Life in Their Hands." I myself have seen the first two of these programmes, and those of my patients and friends who have seen them have nothing but praise and satisfaction in their presentation. I myself thought they were well done and made a responsible contribution to health education in its widest sense. Many patients have told me that they were solaced and comforted by the realization these television programmes brought to them of the great care and skill and kindness that were available in hospitals up and down the country; indeed, the only adverse criticism that I have heard was from those who have not seen the programmes.

The first programme was on Tuesday, February 11, and therefore one can but assume that the leading article in the *Journal* dated February 15 (p. 388) was written before the author had seen any of the programme. It seems to me that the leading article could do nothing but harm to the profession and the Association, an opinion that is borne out by even the most cursory survey of the press comments. The view is outmoded that medicine and those who practise that profession should be shrouded in mystery and awe. If there has been any sensationalism it has appeared only in the *Journal*; it is the last charge that could be levelled against this carefully produced factual documentary of the B.B.C. This opinion is confirmed by this morning's *Manchester Guardian* (February 20): "Some doctors perhaps believe that the less patients know about what is wrong with them the better; a naive and incurious faith in the art of Medicine and the wisdom of its practitioners is the prepared state of mind."

I know that the B.B.C. has taken expert and responsible advice on each of these programmes, and indeed at the earliest stages of the general planning of the series. If it were not for the absurd rule of anonymity one would find in each of these programmes that some of the most distinguished consultants and specialists in the region involved have helped the B.B.C. greatly in the presentation. I should have thought that we in a profession should welcome this move by the B.B.C. and offer it every co-operation rather than this unfounded out-of-date obscurantist criticism in the Association's own *Journal*.—I am, etc.,

Bournemouth. O. C. CARTER.

SIR,—Your leading article with this title (*Journal*, February 15, p. 388) is based on an erroneous idea that live operations are to be televised. At the press conference for medical representatives of the press, these ten programmes were discussed fully and the ways in which further programmes might deal with other aspects. I am sorry you did not send a doctor to contribute to this discussion, for I am sure the B.B.C. would have been glad to hear his views.

You imply that it is doubtful whether it was a good thing that, after seeing "The Hurt Mind" series, many people went to their doctors. This seems to me a good result. They may have gone asking for E.C.T., but surely this gave the G.P. a wonderful opportunity for explanation and allaying their fear—that they were going mad. And I think it likely that they had had this fear before and had not gone merely because, before seeing the programmes, they thought that nothing could be done for their unhappiness.

As regards the present series of ten programmes, I note that the *Sunday Times* considers the first programme "a serious study of current medical research and extremely well done," and the *Observer* "T.V. documentary at its most serious and responsible . . . genuinely uplifting." I can think of further programmes and series of programmes I hope the B.B.C. will do, but I welcome this series because it will increase the information the public has about how their bodies work—much physiology will be conveyed in describing how the operations and machines help disordered bodies—and such knowledge will help all of us who are interested in encouraging people to keep healthy.—I am, etc.,

London, S.W.1. RONALD MAC KEITH.

SIR,—I was amazed to read your leading article in the *Journal* of February 15 (p. 388). I looked in on the programme "Your Life in Their Hands" on Tuesday evening, February 11, with the greatest interest and approval. My patients who saw this programme were loud in their praises, and, far from feeling frightened and neurotic, derived immense comfort and reassurance from it. If the B.M.A. disapproves of this television series—which I can hardly credit—then we should cease publication of *Family Doctor* at once. Good luck to the B.B.C. and to *Family Doctor* in their valuable work.—I am, etc.,

Woodford Green, Essex. ST. GEORGE B. DELISLE GRAY.

*** The Council's resolution on television appears at p. 91 of this week's *Supplement*.—ED., *B.M.J.*

Side-effects of Medical Propaganda

SIR,—With the rapid advance of chemotherapy, doctors are being more often warned that the increasingly complicated substances being introduced are not always free from side-effects. These can be dangerous, and the warnings are wise. It seems a pity that the side-effects of some medical propaganda are not as fully appreciated.

In a recent issue of *Family Doctor* a booklet was enclosed, entitled "Smoking, the Facts." No one will doubt the good intentions which prompted this, nor those behind the anti-smoking campaign of the Central Council for Health Education. Yet one learns from talking to patients that a result of such publicity is an increase of cancer fear out of proportion to the changes wrought in smoking habits.

In psychiatric work anxiety is by far the most common symptom, and anything that may increase this, or even give it a fixation point, must be harmful. The use of threats and the instilling of fear are seldom constructive, and the effects of suggestion, to which neurotics are prone, often exacerbate their sufferings. It seems to me, therefore, that such a policy is unwise, even if, occasionally, it may be effective.

Perhaps it is advisable to lay certain findings and opinions on questions of general hygiene before the public in a simple way, but when this is done it might well be indicated that a talk with the family doctor on the subject would be a good thing, instead of issuing frightening warnings without the advantage of objective discussion.—I am, etc.,

London, W.1. WILLIAM MOODIE.

"The Hurt Mind"

SIR,—As I was medical adviser to the B.B.C.'s recent "Hurt Mind" television series, and as I have also on rare occasions appeared anonymously on such programmes, I hope I may be allowed to reply to some of your editorial strictures (*Journal*, February 15, p. 388) on those who advise on and take part in them. We have, I think, as high a sense of public responsibility as you obviously have, Sir. We know only too well the tremendous power of television for good or evil in matters of medicine, and I do not think that, so far, this power has been greatly abused. Unfortunately, in clinical practice, whether we like it or not, one only too often finds that when any new treatment is suggested to a frightened patient and his relatives, if one can also say that the treatment has been recently written about in the newspapers or discussed on the radio, this often gives it a much better chance of ready acceptance by the patient. And the unlimited faith of the ordinary man in what he sees, especially on the B.B.C.'s television service, can sometimes be truly frightening. Here we have an educational medium of tremendous power in medicine which we should certainly not antagonize, but seek to co-operate with it if the welfare of our patients is our primary aim and purpose.

Your leading article criticized the "Hurt Mind" series because numbers of patients as a result of it got in touch with doctors afterwards to inquire about E.C.T. You also criticize the B.B.C. for dramatizing diseases rather than dwelling on the prevention of disease and on the means of maintaining good health. But are not most of us in medicine dealing most of our time with disease processes? And are not diseases what patients mostly come to us complaining about and wanting help for? Over 5,000 people each year are now killing themselves in this country, many in states of recoverable depression. And if we can only get some of these tragic people to go to their doctors in time and ask about E.C.T., which may prevent suicide, was this really a very wrong thing to do in the "Hurt Mind" series?

Because of the enormous interest aroused by this series, a special and detailed audience research report was made on "The Hurt Mind" by the B.B.C., and it makes very interesting reading indeed.[1] The following extract shows something of what was actually achieved as regards treatments in psychiatry:

> "The most striking of these [changes] was a substantial increase in viewers' confidence in the value of electric shock treatment (before the series, 45% were confident that it would be a 'good thing,' and 65% after), and a corresponding increase in approval of it as a method of treatment (60% before and 77% after). There was also an increase both in confidence and in approval (29% to 48%) concerning leucotomy. . . . 'Group therapy' also gained in terms of public approval (50% before and 64% after), as did 'talking it out under the influence of ether' (38% to 50%) and 'giving them drugs and injections' (47% to 55%). The gains for group therapy and for abreaction seem each to be dependent largely upon the series' telling people what the treatment was, whereas such gain as occurred in respect of 'drugs and injections' was largely the result of conversion from disapproval to approval. . . . From all of this, the picture which emerges is one of a moderate but widely based increase in viewers' confidence that modern medical methods can cure mental illness—an increase which occurs against a background of already considerable confidence."

It was also very interesting to find that there was no increase in approval of individual psychotherapy and psycho-analysis as acceptable methods of treatment to the public. But this was probably in part because previous film and radio publicity had already raised public approval of the use of psychotherapy and psycho-analysis as acceptable treatments in psychiatry to as high as 86% and 70% respectively. The likely accuracy of this report is shown, for instance, by the previous somewhat lower public appreciation given to psycho-analysis as opposed to other more general forms of psychotherapy.

I should also like to pay my tribute to the almost obsessional care for medical accuracy attempted by the B.B.C., in this particular series at least, and to their insistence on consulting every shade of psychiatric opinion so as to try and present a fair all-round picture of the problem to the public. I found them considerate of every requested alteration made to them for medical reasons, and very much aware of the tremendous power for medical good or evil inherent in the producing of such a programme series. I found all concerned constantly asking themselves whether or not the showing of such and such an incident would be likely to upset or have a bad effect on the public, and I certainly saw no evidence that medical accuracy was ever sacrificed simply to obtain dramatic or entertainment effect—rather it was always exactly the other way round. Finally, Sir, I am glad to see we at least seem to have satisfied the Ministry of Health. In a second issue, in which you again criticize these medical television programmes (*Journal*, February 22, p. 449), you also tell us in your medical news column (p. 472) that the Ministry is issuing four specially prepared film telerecordings taken from the "Hurt Mind" series, and you also quote the Ministry's hope that local authorities and others will hire and use these "to further the spread of the more enlightened attitude towards mental illness which the T.V. programmes did so much to foster."—I am, etc.,

London, W.1. WILLIAM SARGANT.

REFERENCE

[1] *The Hurt Mind: An Enquiry Into Some of the Effects of Five Television Broadcasts about Mental Illness and its Treatment*. Audience Research Report. B.B.C. May, 1957.

Acute Otitis Media

SIR,—In your leading article on acute otitis media (*Journal*, February 8, p. 328) you discuss the valuable results of a recent Medical Research Council survey on acute otitis media in general practice. I can confirm from our experience at the Institute of Laryngology and Otology the seasonal incidence of acute middle ear infections with a peak period in the early months of the year. This pattern, however, may be disturbed by unexpected secondary peaks. It can also be confirmed that the number of patients referred to our associated hospital with acute suppurating otitis media has been falling off although the number of

what is termed acute catarrhal otitis media has remained practically steady in the five years 1952 to 1956. Nevertheless our figures have remained higher than the survey's "one per cent." of patients referred for hospital treatment would seem to suggest.

Suppurating	Acute Otitis Media	Catarrhal Acute Otitis Media
1952	1,443	463
1953	1,368	659
1954	911	502
1955	697	494
1956	806	533

I would have welcomed some recommendation on the terminology and diagnostic criteria which have not been entirely clarified in the survey, because in the course of a systematic study of the bacteriology and histopathology of otitis media[1 2 3] we have met with terminological obstacles making the correlation of clinico-pathological findings somewhat difficult. In our experience the overall incidence of the predominant organisms has not varied greatly, but we have been puzzled by the comparatively low incidence of *Streptococcus pneumoniae* in the material studied.[4] A comparative study in general practice would, I suggest, be very valuable. Routine sectioning of bone chips removed at recent mastoidectomy operations and the study of experimentally induced otitis media in the guinea-pig have revealed no fundamental change in the pathology of otitis media either. It might be interesting to section material from all cases of cortical mastoidectomies. I would like to end by supporting the view of your leader writer that "this report suggests another investigation." And may I add: with the co-operation of hospital E.N.T. departments and pathologists ?—I am, etc.,

London, W.C.1. I. FRIEDMANN.

REFERENCES

1 Friedmann, I., *J. Laryng.*, 1955, **69**, 27.
2 —— ibid., 1955, **69**, 588.
3 —— *J. clin. Path.*, 1956, **9**, 229.
4 —— *Proc. roy. Soc. Med.*, 1957, **50**, 406.

SIR,—I was pleased to see your leading article on acute otitis media (*Journal*, February 8, p. 328) and to notice that deafness is emphasized as an important sequela. This deafness may persist for a very long time and is very often (if not always) due to a sterile collection of fluid in the middle ear and eustachian tube which provides an ideal culture medium for further attacks of infection, often without discharge. This is the condition known as serous otitis. It is not characterized by severe deafness, and unless careful attention is paid to both the hearing and also the mobility of the tympanum after an acute attack many cases, especially in children, will be missed. The fluid in children is more often thick mucus rather than the thin straw-coloured fluid seen in adults. The treatment of these cases is a paracentesis or stab puncture of the tympanum, followed by suction, because only then can the middle ear be ventilated and, as a result, the elasticity of the drumhead will be returned quickly to normal. Stirk Adams[1] in his report on the treatment of cartarrhal deafness by irradiation of the nasopharynx made no mention of serous otitis as a cause of deafness, but he did stress the dangers of irradiation, particularly in children, in view of the possibility of leukaemia resulting according to American writers. We in this country have paid too much attention to the lymphoid tissue in the nasopharynx and tubal regions and too little to the important condition of serous otitis. Aschen[2] states, "In agreement with Eggstone and Wolff it has been impossible to find any histological evidence . . . to indicate that the lymphoid tissue of the nasopharynx ever extends as far as *still less invades* the pharyngeal orifice of the tube." Hantman[3] states about serous otitis, "It must be assiduously searched for . . . for here is a golden opportunity for reversing pathology before changes render the process irreversible with permanent hearing damage." In my opinion all cases with deafness after acute otitis media should be referred to a consultant who can then decide whether removal of adenoids, with or without a paracentesis, is necessary.—I am, etc.,

Bath. DAVID STEVENS.

REFERENCES

1 Adams, W. S., *J. Laryng.*, 1957, **71**, 565.
2 Aschen, Gunnar, *Acta oto-laryng.*, 1954, **44**, 295.
3 Hantman, I., *Bull. N.Y. Acad. Med.*, 1952, **28**, 817.

Informal Admission of Mental Defectives

SIR,—I was interested to read the letters of Dr. W. A. Heaton-Ward and Dr. M. P. Nelson (*Journal*, February 8, p. 338). I was surprised at their interpretation of the recent Ministry circular H.M.(58)5 recommending the informal admission of suitable cases of mental defectives and the review of patients already in hospitals (*Journal*, January 25, p. 212). There seems to be no shadow of doubt that a vast majority of patients should remain informally; it seems ludicrous, to say the least, to go through the re-certification ceremony and bring into hospital two magistrates and a clerk to certify patients who are obviously in hospital because they can be nowhere else. This, in my opinion, will not only do away with this farcical procedure, but it will decrease a great deal of unnecessary work of having to write out certificates, and afford the doctor more time for more important clinical matters.

If I read the circular correctly, we are not asked to discharge from Order patients who in the opinion of the medical superintendent should remain under Order. This I think is not only a step forward in the right direction but one of the most welcome documents the mental deficiency service has had for a long time.—I am, etc.,

Balderton, Notts. E. FISCHER.

Breast-feeding

SIR,—Drs. F. E. Hytten, Jessie C. Yorston, and A. M. Thomson are to be congratulated on their informative and unbiased study of breast-feeding (*Journal*, February 8, p. 310). The conclusions reached deserve most serious consideration, particularly when they say, "It is quite clear that both mothers and babies did better with bottle-feeding."

The time appears to have come when the antagonism to bottle-feeding which is so widespread in the profession will have to be reassessed, particularly in hospitals, as so many confinements are now hospital confinements. In maternity hospitals innumerable hours are spent by nurses persuading mothers to breast-feed; and, while this time would be very well spent if it resulted in a contented mother and a contented breast-fed baby, all too often, within a few days of discharge from hospital, the baby is being bottle-fed; and this, very often, in spite of the general practitioner's and the district nurse's further attempts to persuade to breast-feed.

More thought must be given to the problem of which babies are to be breast-fed and which bottle-fed, and, in view of the conclusion of Drs. Hytten, Yorston, and Thomson quoted above, it would appear that the aim should not be to discharge all babies from hospital breast-fed. Perhaps if more babies were sent home from hospital bottle-fed a vast number of mothers would be saved the frustration, anxiety, and unhappiness that they so often endure during their first week at home.—I am, etc.,

Edinburgh, 11. A. GORDON GROSSETT.

SIR,—I wish to comment upon the article by Drs. F. E. Hytten, Jessie C. Yorston, and A. M. Thomson (*Journal*, February 8, p. 310), entitled "Difficulties Associated with Breast-feeding." It was a report of an investigation carried out for the Medical Research Council by three members of the obstetric medicine research unit at Aberdeen Maternity Hospital. Professor Dugald Baird is the honorary director of this unit and gives "his help and criticisms" to its deliberations. The investigators were a nutritionist, a professional researcher, and a lady doctor.

Since the *British Medical Journal* is read in many countries, it is desirable to point out with the least possible delay that the majority of men and women in the British

Isles will resent the implications in this report. In the discussion, we read dogmatic statements for which there is no supporting evidence. This investigation amounts to a classification of the symptoms of inadequate organization for the care of young mothers and babies; there is no contribution to the solution of the main problem, its causes, or its avoidance. It appears to be a further attempt to denigrate the efficacy of the natural processes of healthy motherhood similar to that which was made by the same unit in August, 1956.[1] The purpose of this disparagement of a natural function might be obscure if the ultimate goal of mechanistic materialism in childbirth were not so obvious. The laws of Nature are blamed because the social structure is faulty. No reference is made to the antenatal preparation or the conduct of labour; there is no mention of interference without clinical indication. These matters profoundly influence a woman's desire and ability to feed her baby at the breast.

We can forgive a quota of failures in women and in breasts, but we do not forgive lightly calculated slurs upon the most cherished gift of motherhood in order to hide the ineptitude of those who should be responsible for its felicitation. May our colleagues overseas be assured that this treatise does not represent the considered opinion of experienced obstetric and paediatric clinicians.—I am, etc.,

Chichester, Sussex. GRANTLY DICK-READ.

REFERENCE

[1] Scott, E. M., and Thomson, A. M., *J. Obstet. Gynaec. Brit. Emp.*, 1956, **63**, 331.

First Tuberculosis Dispensary

SIR,—I have followed the recent correspondence on the first tuberculosis dispensary with interest. The latest claim for priority is for the Liverpool Street dispensary, founded in 1848.

I have in my possession *The Medical Guide*, by Richard Reece, M.D., published in London in 1897 (4th ed.). In this work ("for families and young practitioners") the author describes the foundation of a *Phthisical Dispensary* on March 20, 1805, at 70, Chancery Lane:

"Of Consumption of the Lungs.

"So prevalent and destructive is this disease in Great Britain, that it is calculated to destroy no less than sixty thousand of its inhabitants annually, the majority of which is supposed to be under twenty-five years of age. The great consumption of animal food and vinous or spirituous liquors in a climate so mutable, may in some degree account for its frequency, while the melancholy fatality is more to be attributed to the imperfection of the healing art than the absolute incurable nature of the disease; indeed, so generally, has this latter opinion prevailed, that the palliation of symptoms has been the chief object of practice, and on this account indigent consumptive patients have been deemed improper objects of the different charitable institutions established throughout the kingdom, for the relief of the poor afflicted with disease; in consequence of which they fall an easy and cruel sacrifice to the nostrums of unprincipled quacks.

"These circumstances, together with the conviction that consumption of the lungs, in certain stages, is a curable disease, induced me to undertake the establishment of a *Phthisical Dispensary* in conjunction with Mr. William Roberts (an able surgeon in London), for the relief of consumptive patients only, which the liberality of his Royal Highness the Prince of Wales, and several leading characters in the kingdom, soon enabled us to carry into execution. The number of patients that have already been discharged cured, and apply every week for admission, convince me that it will prove of greater national advantage than was first imagined, and it is to be hoped that its resources will increase with its reputation."

Subscribers of one guinea per annum were entitled to recommend three patients each year, and these patients were "supplied with medicines and advice gratis." A preparation of *Lichen islandicus* is favoured by the author. The value of fresh air is admitted, and a quiet life and nutritious diet (to include plenty of milk) is advised. The author does not claim specifically that this was the first institution of its kind, so perhaps there were others before it. I know nothing of its subsequent history.—I am, etc.,

Greenwich, S.E.10. A. R. ROBERTSON.

SIR,—Drs. W. Hartston and W. F. Wheeler (*Journal*, February 8, p. 339) are to be congratulated on their interesting letter on the founding of the Liverpool Street Chest Dispensary, and the City of London Hospital for Diseases of the Chest. These institutions no doubt did the best that could be done for chest patients in the days before Robert Koch. According to the custom of the time, they were named "dispensaries," because their principal service was dispensing drugs.

Sir Robert Philip, when he opened his Edinburgh centre in 1887, carried on the old term "dispensary." But to imagine this had anything in common with the older foundations but the name is to confuse words with things. Philip's revolutionary ideas upon prevention and treatment completely outmoded the old "dispensary." He put Koch's discovery into practical medicine by treating the tuberculous patient as the infective agent in the family and community. Drug treatment was subordinate: the social rehabilitation of the patient was all-important. There was a world of difference between Philip's outlook (and that of every modern chest clinic), and that of the older chest dispensaries. Lloyd's coffee-house was the predecessor of the insurance market called Lloyd's; they use the same title, but they are not the same thing. The places where John Hunter operated without anaesthesia or antiseptics were hospitals; but how different from post-Listerian centres of surgery!

Those London institutions mentioned by your correspondents, though excellent by the standard of their time, were pre-Koch and pre-Philip, and were not "tuberculosis dispensaries." They do not invalidate Philip's claim to have founded the first tuberculosis dispensary in the modern sense.—I am, etc.,

London, W.C.1. HARLEY WILLIAMS.

Ulcerative Colitis

SIR,—Your summary dismissal of the ileo-proctostomy operation in your leader on ulcerative colitis (*Journal*, December 21, 1957, p. 1479), with the concluding remark that this choice of operation be reserved for those unable to manage a permanent ileostomy, such as "children and the feeble-minded," prompts me to register in the strongest terms my disapproval of your views, which I regard as old-fashioned and retrograde. I sincerely hope that, after reading this letter, doctors contemplating surgery for their cases of ulcerative colitis will instead give first consideration to the ileo-proctostomy, leaving a permanent ileostomy as very much a second choice. To advocate such an unpleasant disability as a permanent ileostomy as first choice is, in my view, quite wrong at a time when the ileo-proctostomy is being performed at the Gordon Hospital for Rectal Diseases, and elsewhere, with such remarkable success.

My wife was admitted to the Gordon Hospital in June, 1954, in a moribund condition. Medical treatment at another hospital had failed to stem the tide of an acute fulminating form of this disease. A total colectomy with a temporary ileostomy was performed, and for a period of three months the rectum was given time to settle down and heal, and the patient a chance to recover a reasonable state of health, following which the ileo-rectal-anastomosis was carried out. Here, therefore, is one patient who can compare and contrast her present condition with life as it might have been with a permanent ileostomy. She enjoys wonderful health and is at the moment having to diet to curb her proportions. She eats anything and everything she likes, and she has never felt so well in her whole life. She has, as a rule, not more than four or five bowel movements daily, can go as long as 12 hours or more without the need for a bowel movement, and is only rarely disturbed nocturnally. She has become so accustomed to her new bowel habits that she is no longer aware of them, and does not for a single moment regard herself as being in any way incapacitated. This process of adaptability occurred rapidly within the first six months, and has continued

gradually ever since. My wife still recalls the nuisance of stubborn constipation in the days before she became acutely ill, and she is in fact grateful to-day that constipation is something from which only other people suffer.

We both remain ever grateful for the opportunity my wife has had to enjoy life without a permanent ileostomy, through the good fortune of being No. 17 in Mr. Stanley Aylett's series of cases.[1] Far too many people, both doctors and patients alike, are unfamiliar with his, and his colleagues', work in the surgery of this disease, and may not be aware that in selected cases there is now a wonderful alternative to life with a permanent ileostomy.—I am, etc.,

Leeds, 17. H. M. MICHAELSON.

REFERENCE

[1] Aylett, S., *Brit. med. J.*, 1957, 1, 489.

Amnion Implantation in Peripheral Vascular Disease

SIR,—The recent publications on amnion implantation in peripheral vascular disease, first from Mr. H. Dendy Moore (*Journal*, December 7, 1957, p. 1350) and secondly in your correspondence column from Mr. E. Troensegaard-Hansen (*Journal*, January 4, p. 39) must have aroused considerable interest amongst those who have a special interest in this subject and also amongst those who often acquire these cases in rather less spectacular ways. It does seem a pity that on such a small number of cases Mr. Dendy Moore has sought to condemn amniotic implantation. The surgeon at the moment has little to offer the sufferer from claudication. Sympathectomy has no sound physiological basis for regular use in such cases. Grafting has only a limited field of application at the moment. Section of the tendo Achillis may apply to farm horses but is scarcely worthy of current surgical philosophy. What have we left to offer?

Troensegaard-Hansen's paper[1] may, I believe, offer a little more hope. The material which I have had at my disposal is quite insufficient to draw any lasting conclusions from. Sufficient encouragement, however, has been forthcoming from cases treated in this way to lead me to believe that the treatment is at least worth persevering with. Indeed the subjective relief in patients on whom I have performed amniotic implantation has been striking to witness. True, we have had no arteriograms and no radioactive sodium to prove its value. When relief, however, is so dramatic it surely seems superfluous to go to such lengths. In any case true scientific investigation is surely the province of the special units. In the meantime many of us who may, perforce, have to manage the care of intermittent claudication will await further publications on this subject with an enthusiasm almost bordering on the emotional.—I am, etc.,

West Hartlepool. A. WEBB-JONES.

REFERENCE

[1] Troensegaard-Hansen, E., *Brit. med. J.*, 1956, 2, 262.

SIR,—Amnion implantation for peripheral vascular disease may offer a simple procedure for the relief of what is, on the whole, a difficult condition to improve by surgery. The results, therefore, are of great interest at the present time. Mr. H. Dendy Moore (*Journal*, December 7, 1957, p. 1350) reports a series of seven cases with complete failure in each, in contrast to Mr. E. Troensegaard-Hansen's final 20 cases, all of which showed complete relief of symptoms.[1] Dr. W. F. M. Unger-Hamilton's letter (*Journal*, February 1, p. 281) mentions further successful cases. The success of the method is therefore still *sub judice*, and it might be of interest to record the results in seven cases treated at the Leicester Royal Infirmary.

If there is, in fact, any specific action of amniotic tissue in improving the circulation, it seemed more logical to use fresh untreated amnion obtained at caesarean section, and in this hospital we were able to do this, the graft being implanted in a neighbouring theatre within a few minutes of obtaining it. No attempt was made to remove the chorionic tissue, and in these two respects the technique differed from both Mr. Troensegaard-Hansen's and Mr. Dendy Moore's series. Of the eight cases treated, the results of one were invalidated by subsequent sympathectomy for threatened gangrene. The remaining seven cases had suffered from intermittent claudication only, without any trophic changes. Our results are tabulated below.

In no case were the symptoms abolished, but all except one case were improved. It was noted that, while the claudication persisted in all six cases, the walking distance was increased and the ensuing stopping time was diminished. The severity of the claudication pain was lessened, and most patients considered this to be of most help to them.

In considering these results, the follow-up period is far too short for a final assessment, and the subjective element

	Age	Date of Implant	Pre-operative Walking Distance* and Stopping Time	Present Walking Distance* and Stopping Time	Other Factors	Subjective Result	Objective Result
A. H.	70	22 7 57	1½ miles	2 miles	Diabetic (18 units daily)	"Pleased"; "improved"	Definite improvement
			10 minutes	Does not stop; pain much less severe			
T. F. B. . .	54	22 7 57	100 yards	200 yards	Old T.B.	Fairly pleased; "certainly better than it was"	Some improvement
			10 minutes	5 minutes			
G. E. L. . .	59	18 11 57	75 yards	100 yards +	Severe bilateral varicose veins	Pleased with operation; "big improvement"	Some improvement, possibly temporary
			10 minutes	2 minutes; pain much less severe			
J. H. B. . .	55	18 11 57	250 yards	No claudication	Patient had a sympathectomy immediately following his graft	The result therefore is largely obscured	
			5 minutes	—			
T. S.	61	18 11 57	350 yards	250 yards	—	Some improvement, "operation worth while"	Graft probably not effective
			5 minutes	5 minutes			
R. A.	61	22 7 57	50 yards	800 yards	Angina of effort 4 years	Pleased; "25% improvement"	Definite improvement
			3 minutes	1 minute. Pain much less severe			
T. D.	72	22 7 57	20 yards	800 yards	Moderately severe varicose veins. Moderate osteoarthritis	Pleased; "well worth doing"; "a deal of benefit"	Definite improvement
			10 minutes	Pain less severe; could keep on walking with difficulty			
J. S. M. . .	53	18 11 57	400 yards	600 yards	—	Definite improvement	Probably slightly improved
			4–5 minutes	Pain less severe; stops only momentarily			

* 1 yard = 0·9 metre. 1 mile = 0·6 km.

is difficult to eliminate without a much more thorough investigation than we have facilities for.

We feel that in this small series the results are sufficient to warrant an extended trial of the method.—I am, etc.,

Leicester. J. THOMPSON ROWLING.

REFERENCE

1 Troensegaard-Hansen, E., *Brit. med. J.*, 1956, **2**, 262.

Enanthem of Glandular Fever

SIR,—With reference to the article entitled "Enanthem of Glandular Fever" by Drs. F. I. Caird and P. R. Holt (*Journal*, January 11, p. 85) and the discussion therein of the differential diagnosis of palatal petechiae, I feel that it should have been definitely stated that the palatal rash in scarlet fever is occasionally petechial. This appears to be analogous to a similar occasional occurrence in certain areas in the skin in this disease. Nevertheless, it usually occurs in cases not showing petechiae elsewhere.—I am, etc.,

Croydon. J. J. LINEHAN.

Resuscitation

SIR,—I was surprised to read Dr. O. P. Llewellyn (*Journal*, January 4, p. 42) questioning the effectiveness of mask ventilation in connexion with the "Stephenson Minuteman Resuscitator." In this hospital we make use of mask ventilation daily for poliomyelitis patients who have little or no ability to breathe. We use an Oxford inflating bellows worked by hand. Ventilation is satisfactory at all times. By this method a poliomyelitis patient has been ventilated throughout an ambulance journey lasting three hours. Occasionally also we use mask ventilation for unconscious poliomyelitis patients. At no time has there been any clinical evidence of air entering the stomach, though it is possible that small amounts did so on occasion.—I am, etc.,

Pill, near Bristol. R. V. WALLEY.

Recurring Cystitis in Women

SIR,—Mr. H. P. Winsbury-White's further observations on recurrent cystitis in women (*Journal*, December 14, 1957, p. 1399) should arouse considerable interest, for undoubtedly this condition is neglected all too frequently or treated empirically by many sections of the medical profession. Gynaecologists rank prominently among those who share this responsibility, for disturbances of micturition are among the commonest of gynaecological complaints. It is therefore surprising and regrettable that cystoscopic procedures figure infrequently—and urethroscopy but rarely—upon gynaecological operating lists.

In the treatment of gynaecological conditions associated with urethro-vesical symptoms incomplete investigation of the urinary tract is the rule. Faith may be misplaced in bacteriological reports upon catheter specimens of urine sent for examination (and examined, perhaps, many hours later); but residual urine estimation, cysto-urethroscopy, etc., are rarely performed. In defence it may be claimed that cure of the urinary symptoms usually follows treatment of the gynaecological lesion; but the urethro-vesical cure is all too often incomplete and temporary. Surely it is as illogical for gynaecologists to ignore the precise state and necessary treatment of the urinary tract when treating cervicitis as it is for urologists to ignore associated cervicitis when dilating and cauterizing chronic urethritis.

Other examples could be cited to illustrate my conviction that Mr. Winsbury-White's article presents a challenge to gynaecologists to hand over a large proportion of their cases to their urological colleagues for correct investigation and treatment. The only alternative is a reorientation—long overdue—whereby gynaecologists come to realize that the cystoscope is second in importance only to the curette in the armamentarium of a competent gynaecologist. To the old facetious dictum that "the efficiency of a gynaecological unit is inversely proportional to its ventri-suspension rate" let us add "and proportional to its cysto-urethroscopy rate"!—I am, etc.,

Natal. DERK CRICHTON.

Common Cold: Fact or Fancy?

SIR,—I venture to record the following personal observations, as I would be interested to know whether anyone else may have had a similar experience. Last spring, being unable any longer to remain unconvinced by the mounting evidence of an association between smoking and lung cancer, I decided that it was incumbent upon me to act upon it. I therefore stopped smoking and have not started again since. All my life I have been subject to the usual winter colds. In the last ten years in general practice these have constituted a recurring affliction every six to eight weeks throughout the winter months. This year, however, for the first time, I have not had a single cold. This has been such a unique experience that I tried to consider what factor might have contributed to it. The only thing that I can think of is my cessation of smoking. Whilst realizing that in one year this may be purely fortuitous, I wonder if anyone else has had a similar experience.—I am, etc.,

Twickenham. DAVID WHEATLEY.

Treatment of Chilblains

SIR,—While agreeing with everything Dr. Risteard Mulcahy writes in his letter (*Journal*, February 1, p. 281), may I add that a common precipitating cause of chilblains is the sudden immersing of the hands or feet, when cold, in very hot water, as for example when stepping into a bath. Extremities should be warmed up gradually, commencing with tepid water. When chilblains have developed, painting with oil of turpentine gives considerable relief.—I am, etc.,

Aberdeen. R. R. M. PORTER.

Epistaxis

SIR,—Dr. I. H. J. Bourne's letter (*Journal*, January 18, p. 161) prompts me to suggest another method of home treatment. The nose can be plugged with cotton-wool wound round a matchstick *à la* ear mop, but much thicker and moistened with adrenaline or one of the commonly used nasal decongestants. This procedure was forced on me when confronted with a case of epistaxis while completely unequipped (except for a sample of proprietary decongestants), and I found it so simple and effective that I have used it with 100% success ever since.—I am, etc.,

New Romney, Kent. E. LEISER LONBAY.

SIR,—In the recent correspondence on the treatment of nose bleeding, one very valuable styptic seems to have been overlooked. I refer to liq. ferri perchlor. dil. A pledget of gauze or cotton-wool inserted in the affected nostril will nearly always stop the bleeding. The patient is told not to attempt to breathe through the nose. The pledget can be left in for 12 to 24 hours. It should slightly distend the nostril. Where the patient is alarmed, he should be reassured and given, if necessary, a hypodermic injection of morphine, gr. ¼ (16 mg.), and atropine, gr. 1/150 (0.43 mg.). This assures a good night's rest for both patient and doctor. A little petroleum jelly can be smeared in the nostril after removal of the pledget. Liq. ferri perchlor. dil. is equally effective for bleeding after dental extractions. A pledget applied to the bleeding area, covered by as large a wad of cotton-wool as the patient can bite on, will usually stop the bleeding. Also, bleeding from shaving cuts can be stopped instantly by touching with cotton-wool soaked in liq. ferri perchlor. dil.—I am, etc.,

Saxmundham. NOËL STEPHEN.

Pathology Profaned

SIR,—With reference to Mr. I. B. Thorburn's article (*Journal*, January 25, p. 200), I should like to know when it became possible to eliminate pathology, and when it became reversible.—I am, etc.,

Woldingham. J. FABRICIUS.

Buthalitone Sodium

SIR,—I have read with interest the paper by Drs. Peter H. Simmons and May S. Blanshard on buthalitone sodium (*Journal*, December 7, 1957, p. 1347). My own experience with this drug is confined to rectal administration. The principal undesirable feature of hypnotics (barbiturates, paraldehyde, or bromethol) when administered rectally and followed by ether or trichloroethylene anaesthesia is the prolonged recovery period. In view of the statement made regarding the short duration of action of buthalitone sodium an attempt was made to ascertain if the combination of rectal buthalitone sodium and ether anaesthesia would be followed by a short recovery period. The tests were carried out on children who were having manipulations and plasters for the treatment of orthopaedic deformities. Parallel series of 20 cases each were premedicated with buthalitone sodium, 1 g. per 25 lb. (11.3 kg.) of body weight, or hexobarbitone, 1 g. per 30 lb. (13.6 kg.) of body weight, or thiopentone 1 g. per 50 lb. (22.7 kg.) of body weight, all drugs administered rectally in 10% solution. The value of the test was enhanced because in several instances the same children received each of the premedications. When sleep had ensued anaesthesia was induced with ethyl chloride, and continued to a depth of stage 1 with ether. The average anaesthetic duration was 30 minutes.

Children premedicated with thiopentone or hexobarbitone fell deeply asleep in an average of six minutes, and after the termination of the anaesthetic showed first signs of recovery (crying, moving, or opening of eyes) in an average time of 35 minutes. Those premedicated with buthalitone fell asleep in an average of 10 minutes, but the sleep appeared less deep, so that the child was more apt to rouse with the ethyl chloride administration. The first signs of recovery appeared in the same average time (35 minutes). Because of the findings that with buthalitone sleep took longer to supervene, and was lighter, than with thiopentone, while the recovery period was not shortened, it was concluded (as also Drs. Simmons and Blanshard decided) that buthalitone was a less satisfactory drug when administered rectally than was thiopentone. In addition equivalent doses of buthalitone were approximately four times as expensive as thiopentone.—I am, etc.,

Melbourne, Australia. W. H. J. COLE.

Techniques of Psychotherapy

SIR,—Dr. Nigel Walker (*Journal*, February 15, p. 398), commenting on my review of his book *A Short History of Psychotherapy in Theory and Practice*, is good enough to say that his letter is a tribute to the importance of my criticisms. One of these questioned the validity of his assertion that "Jung's uneasiness about the Freudian emphasis on sex was the main reason for his apostasy." Dr. Walker is evidently unaware that Jung, before he met Freud, published his objection to the psychological universality which Freud seemed to attribute to the dogma of the infantile sexual trauma. He was writing in defence of Freud's work: but he made it clear that fairness to Freud did not signify a conditionless surrender to Freud's theories on sexuality. When Jung met Freud for the first time, he took up the same position. This was not, as Dr. Walker states, because Jung "did not like to talk to patients about sex." It was because he found no support for Freud's claims concerning sexuality in his word-association experiments or in his clinical experience. Further, he considered Freud's dogma was too narrow and failed to explain much that needed explanation. Incidentally Dr. Walker makes the common mistake of using the word "sex" when "sexuality" is meant.

It should be obvious to anyone familiar with Jung's writings that the reasons for Jung's divergence from the psycho-analytical school are found in his observations on mental energy (libido) and symbolism. The late Professor Flugel,[1] a distinguished psycho-analyst, recognizing this, is correct in saying that Jung's revolt was by extension—what Freud and others thought an unjustifiable extension—of psycho-analysis. I had the opportunity to discuss the rift between Freud and Jung with Freud himself. He did not mention the matter raised by Dr. Walker, and in fact said that Jung's departure was a great loss.

Dr. Walker, not content to repeat an erroneous statement, goes further: he virtually accuses Jung of dishonesty by stating that Jung's theoretical arguments were probably attempts to confuse the main issue. If Dr. Walker means what he says, his competence as a historian of psychotherapy may well be questioned; if he does not mean what he says the statement should be withdrawn. Dr. Walker, referring to another criticism in my review, still maintains that all modern psychotherapeutic methods are descended from those of Mesmer. I considered he had misinterpreted the facts. Mesmer was not a psychotherapist: he believed in a universally distributed and incomparably rarefied fluid, which by the use of magnets and in other ways passed into the body of the patient and produced benefit. Braid showed the falsity of Mesmer's opinion on animal magnetism and propounded his own belief in the subjective nature of the phenomena ascribed by Mesmer to objective influences. If Dr. Walker can detect traces of Mesmer's conceptions in modern psychotherapy and in Freud's writings, he is of course entitled to his opinion. Braid influenced the French psychotherapists, and certainly Freud was impressed by what he saw at Nancy. Freud also records the profound effect Charcot had upon him. But I am not aware that Freud acknowledged any debt to Mesmer.—I am, etc.,

London, W.1. E. A. BENNET.

REFERENCE

[1] Flugel, J. C., *A Hundred Years of Psychology*.

A Case of Health

SIR,—I feel sure that many of your readers must, like myself, have been stimulated by Dr. Richard's Asher's "case report" (*Journal*, February 15, p. 393), which shines forth from its background of pathology like a good deed in a naughty world. We need more of this kind of thinking and more research into the causes of this type of health to which so many aspire but which so few, alas, achieve.

Dr. Asher observes that this rare condition of health is probably hereditary. Certainly her longevity, physique, and character may well be in part inherited; but this cannot be the whole story. We have all met old people who started out with similar advantages but who have found themselves in old age feeble, lonely, unwanted, and unhappy. To complete the picture of this wonderful old lady one would need to know more about her upbringing and the main events of her life which may have contributed to the physical, mental, and moral toughness which she undoubtedly displays. Now that Dr. Asher has so felicitously reported on "a case of health" could he not place us still further in his debt by letting us have a little more information on aetiology?—I am, etc.,

Bexleyheath, Kent. JOHN LANDON.

POINTS FROM LETTERS

Common Cold

Dr. N. PINES (London, N.W.11) writes: I took part in the discussion ("The Common Cold: Fact and Fancy," *Journal*, January 25, p. 214), and told about a method to prevent colds, verified over a period of 8–10 years and borrowed from the doctors' letters to your *Journal*. . . . When washing your face with hot water and soap, put your soapy fingers as high as possible in your nostrils, paying special attention to the antero-inferior angle. If having a cold, do not blow your nose frequently, sniff up.

Medical Association for the Prevention of War

Dr. DOUGLAS EVERINGHAM (Rockhampton, Queensland, Australia) writes: The above association is not engaged in trying to take peace umbrellas to the Kremlin, but to bring to professional men and the public facts with regard to the semantics and psychology of propaganda, the direct and delayed dangers of atomic fall-out, and other saner approaches to the problems which are too often "solved" by wars and rumours of wars. Anyone who will ask for their publications can convince himself rapidly that this movement is no offshoot of communistic "peace" circuses.

Obituary

G. C. SWANSON, M.B., Ch.B.

Mr. G. C. Swanson, honorary consulting surgeon to the Glasgow Royal Infirmary, died at his home at Balfron, Stirlingshire, on February 7. He was 69 years of age.

George Carson Swanson was born in 1888, the son of Dr. James Swanson, a former professor of biology in St. Mungo's College, Glasgow. After leaving school he worked as an engineer before turning to medicine, which he studied at Glasgow University, graduating M.B., Ch.B. in 1916. After serving in the R.A.M.C. as a surgical specialist at the 47th General Hospital in France in the first world war, he returned to Scotland and became surgeon-in-charge of the orthopaedic wards at the Bellahouston Red Cross Hospital. Subsequent appointments he held included those of extra dispensary surgeon at Glasgow Royal Infirmary, assistant to the professor of anatomy in the medical school of the infirmary, and assistant to the St. Mungo professor of surgery in Glasgow University. Later he became assistant surgeon at Glasgow Royal Infirmary, and ultimately senior surgeon. When he retired from the active staff of the infirmary in 1953 he was appointed honorary consulting surgeon, and those who served under him as house-surgeon during the previous 18 years made him a presentation.

W. R. writes: Mr. George Carson Swanson had a long and distinguished career in Glasgow Royal Infirmary. He was first appointed to the staff in 1919, and from 1935 to 1953 was surgeon-in-charge of wards. Before studying medicine he was an engineer, and his mechanical skill was a feature of his surgical practice. He devised many new instruments which have now become standard, and in his workshop he made those instruments with a precision and quality far superior to routine standards. In the first world war he served as a surgeon in France, and on joining the Royal Infirmary staff became an assistant to Professor Robert Kennedy, and was associated with him in his experimental surgery. As a surgeon he was a master craftsman, and his gentle touch in the theatre was reflected in the smooth and rapid recovery of his patients. As a teacher he was lucid and clear in his lectures, and at the bedside he demonstrated the logical approach to diagnosis. To the nursing staff he was always courteous and friendly, and to his medical staff he was helpful with constructive criticism and friendly advice. He inspired a warm affection in all those who worked with him, and their sympathy is extended to his wife and daughter.

L. A. PARRY, M.D., F.R.C.S.

Dr. L. A. Parry, who was a very well known general practitioner in Brighton and Hove and at one time a member of Council of the B.M.A., died suddenly at his home at Hove on February 19. He was 87 years of age.

It is many years since Dr. L. A. Parry was prominent in council and committees at Headquarters, but the recollection of his personality is still vivid among those who sat with him, and in Sussex few practitioners have engaged the affections of their colleagues to the same extent. His engaging manner and quick mind, his wide knowledge, especially of everything which had to do with the forensic side of medicine and with the contacts of medicine with the State or the local authorities, and his readiness to help a fellow practitioner in any difficulty made him an outstanding figure in his own county. He was always accessible, and no problem was too trivial for his interest. From Hastings to Chichester, whenever any difficulty arose in medical practice or hospital or public health service, the byword was, "Ask Parry of Hove." His greatest service was his 16 years' honorary secretaryship of the Sussex Branch, but he was honorary secretary for many years of the Brighton Division also, and in these and other capacities he served his profession well.

Leonard Arthur Parry was born on May 13, 1870. His medical school was Guy's, and he graduated M.B. in 1894. Two years later he proceeded M.D. and took the F.R.C.S. After some resident appointments at his teaching hospital and elsewhere in London he settled on the South Coast, where paediatrics claimed his special interest. Among the many appointments which he held in Brighton and the neighbourhood were those of surgeon, and afterwards consulting surgeon, to the Royal Alexandra Hospital for Sick Children and the Hove Cripples Guild. He was medical officer to the local Barnardo's Homes, to the Brighton School for Blind Boys, to the Hove Education Committee, and to the Brighton Grammar School. He also acted as medical referee for various assurance companies and as examiner to the St. John Ambulance Association. During the second world war he was group officer in the Emergency Medical Service for the Brighton area.

His first considerable contact with Association affairs seems to have been on the occasion of the Annual Meeting at Brighton in 1913, when he was chosen as honorary local secretary; that highly successful meeting was a proof of his organizing capacity, of which his brethren in the Brighton area were destined to make much further use. He was even then a considerable figure in his specialty, as was shown by his appointment to the vice-presidency of the Section of Diseases of Children at the same meeting. Twenty-five years later he was the bearer of an invitation from his Division to the Association again to visit Brighton for its Annual Meeting, but the war intervened before the invitation could be accepted, and it was not until 1956 that the Association returned to Brighton.

From 1914 to 1921 Parry was assistant honorary secretary to the Brighton Division, and then became full secretary, holding the office until 1928; he was treasurer after that, and chairman of the Division in 1929–31 and again in 1936–7. Parry, with E. R. Fothergill and some others, made Brighton one of the most "live" Divisions in the Association. His honorary secretaryship of the Sussex Branch began in 1922 and continued until 1938, and he was president of the Branch from 1942 to 1949. For about 10 years he was a representative and for four or five years a member of Council.

The Headquarters committees to which he gave his services were numerous. For 12 years he served on the Finance Committee. He was also for many years on the Ethical Committee, and had a good deal to do with the reorganization of the ethical machinery of the Association and with the revision of the rules of procedure governing expulsion cases. He was a prominent member of the special committee which the Council set up to report on psycho-analysis, a piece of work which extended over three years. He had much to do with the shaping of the report on mental deficiency which the Association got out in 1932. He was vice-president of the Section of Medical Sociology at the Annual Meeting of 1923 and again at the Annual Meeting of 1931. His counsel on medico-legal questions was always sought and listened to.

Parry had an astonishing acquaintance with the byways of history—of medical history in particular, as illustrated by the pages of this *Journal*, which in the course of years contained innumerable letters from him or notes under "Nova et Vetera" on the results of his researches, bringing to light many curious and often grim episodes and customs of the past. The titles of his three books indicate the direction in which his researches lay—*Some Famous Medical Trials*, *History of Torture in England*, and *Criminal Abortion*. The last, published in 1932, was an exposition of the facts about abortion, its frequency in different countries, the methods used, and the history of the practice; it did not enter to any extent into ethical considerations. The themes on which in this *Journal* he brought interesting information to light included the execution of children, methods of hanging, spontaneous combustion, illegal operations, prehistoric trephining, curiosities of caesarean section, and, by way of lighter relief, Lambeth degrees. What he stated was always carefully documented and gave evidence of wide and precise reading. On at least one occasion, however, he was caught

out and incurred the wrath of some Scotsmen when, on giving a lecture, reported in these columns, on famous medical criminals, he included among the number the gentle Archibald Cameron, who was medical officer in the army of the Pretender. He treasured a letter which he received from the late Sir Dawson Williams: "Here you are again making trouble—not this time with a harassed editor, but with a Highlander who in the eighteenth centry would probably have called upon you with his claymore newly sharpened." The editor added, however, that by means of a suave editorial note he had probably lessened the tension. In addition to these historical excursions Parry wrote various papers on surgical subjects and also on the risks and dangers of certain occupations and their prevention.

The passage of years and a life of hard work never seemed to take undue toll of him, and he retained into old age a certain boyish eagerness and zest. He will be greatly missed.

R. S. TRUEMAN, M.B., B.Sc., F.R.C.S.Ed.

Dr. R. S. Trueman died at St. Bartholomew's Hospital on Christmas Day, 1957. He was 54 years of age.

Raymond Shaw Trueman was born on May 2, 1903. After obtaining the B.Sc., with honours in engineering, from London University in 1925, he began the study of medicine at St. Bartholomew's Hospital, qualifying by taking the London Conjoint diploma in 1931. Two years later he graduated M.B., B.S., and in 1937 was elected F.R.C.S.Ed.

D. H. S. writes: After qualification Dr. Trueman travelled as a ship surgeon, and, having found a charming South African wife, went to live, first at East London and, later, in Salisbury, Southern Rhodesia, where he specialized in proctology. Then signs appeared of the illness which eventually caused his death, and he returned to this country in 1951, to Amesbury, Wiltshire. He made many friends. He loved meeting people, and he trained himself to become a most interesting conversationalist. His early training as an evangelical Christian gave purpose and direction to a life characterized by unselfish devotion to God and to his fellow men. He was always fond of young people, and founded the Crusader Class at Snaresbrook, Essex, in 1926, which is still flourishing, and, later, a similar class at Salisbury, Southern Rhodesia. When finally he made his home at Amesbury he founded the Salisbury Plain Christian Fellowship, and he and his wife made an excellent host and hostess to many a lonely soldier from the camps who needed friendship and counsel (and food !), and oft-times a word of guidance from the Holy Scriptures. With great courage and selflessness he faced the inevitable end. His wife and his aged mother survive him, and much sympathy is extended to them in this great loss.

F. J. R. STONEHAM, F.F.A.R.C.S.

Dr. F. J. R. Stoneham, consultant anaesthetist to the Windsor group of hospitals, died at the Canadian Red Cross Memorial Hospital, Taplow, on January 14. He was 48 years of age.

Frederick James Russell Stoneham was born at Weymouth on February 24, 1909. He was educated at Harrow School, and received his medical training at Guy's Hospital, qualifying M.R.C.S., L.R.C.P. in 1937. He then held a series of resident posts at Guy's Hospital, finally becoming anaesthetic registrar. In 1941 he joined the Royal Air Force and was immediately employed as an anaesthetist. He attained the rank of squadron leader, which he held until demobilized in 1945. Having obtained the D.A. of the English Royal Colleges, he was then appointed senior anaesthetist to the Birmingham Accident Hospital, where he was also in charge of the shock and resuscitation unit. This period influenced his future work, as he never failed to apply his extensive knowledge of shock to the care of his patients. He was particularly interested in anaesthesia for children, with whom he was most understanding, quickly gaining their confidence. His attention to detail and his obvious enthusiasm for his work gained for him the respect of his colleagues. In 1948 he moved to Windsor and was appointed anaesthetist to the Windsor group of hospitals. In 1950 he was graded consultant anaesthetist to the Windsor group, his main work being carried out at Maidenhead Hospital, Heatherwood Orthopaedic Hospital, Ascot, and the Canadian Red Cross Memorial Hospital, Taplow. In 1956 he was elected F.F.A.R.C.S. While at Windsor he took part in the investigation of "plasmosan" in the treatment of shock, and wrote a paper on the subject. He also wrote an article for *Anaesthesia* in 1950 on an improved jaw support. He was devoted to his family and his home. To his work he gave much thought and care, constantly striving to improve the standard of anaesthesia. He gave to his patients the same kindness and consideration which made him so many friends. The world is a poorer place for his passing, and with his widow and two daughters we mourn the loss of a friend.—G. P. A.

JAMES HOWARD, M.R.C.S., L.R.C.P., D.P.H.

Dr. James Howard died at his home at Hyde on February 1 after a brief illness. He was 80 years of age.

J. K. writes: With the death of Dr. James Howard, the busy little industrial town of Hyde in the north-east corner of Cheshire has lost its senior practitioner. Born in Hyde, he had practised for over fifty years in his native town, where his father, Dr. Robert Howard, had practised for upwards of fifty years before him, and the tradition of good family practice is continued by his son, Dr. J. Brian Howard. James Howard, who was born on November 18, 1877, studied medicine at Owens College, Manchester, and his clinical work was done at the old Manchester Royal Infirmary in Piccadilly. He qualified M.R.C.S., L.R.C.P. in 1903, and two years later took the Manchester D.P.H. After qualification he was house-physician to Dr. Graham Steele, honorary physician to the Royal Infirmary. A house appointment was not in those days so common a procedure for the young doctor, but this intern appointment gave him an intensive and practical experience of medical practice which proved of great value in subsequent years. He remained a careful and efficient diagnostician. He was courageous in treatment, for in the early days of this century the general practitioner was called upon to undertake duties which are now relegated to the hospitals. In the first world war Dr. Howard held a commission in the R.A.M.C. from 1915 to the end of the war. He was with the 2/1 North Midlands Field Ambulance and was attached to the Sherwood Foresters. The greater part of his Army service was in France, and while serving on the Western Front he suffered seriously in a gas attack.

A member of the British Medical Association for nearly forty years, he served a very successful year in 1930 as chairman of the Hyde Division. He took an active part in the social and cultural activities of the town, its charities and sports, but it is as a good family doctor that his memory will remain. He was beloved by his patients and highly esteemed by his colleagues. Tall and slim in stature, he gave confidence to his patients. His presence did them good. He was popularly known as "Jim" Howard, a term of affection rather than familiarity. He was particularly happy in his home life, and our sympathy goes to his widow and son who shared a life in a busy industrial practice—a life worth living.

R. W. CUNINGHAM, M.B., B.Chir.

Dr. R. W. Cuningham, who succeeded to his father's practice in Londonderry in 1929, died at the City and County Hospital there on January 25, aged 56.

Ronald William Cuningham was born on June 5, 1901, the son of the late Dr. H. W. Cuningham. He was educated at Foyle College, Londonderry, and, later, at Warwick College. In 1914, after the outbreak of war, he and his brother, while still schoolboys, were interned in Germany while there on holiday, but were repatriated in

October of the same year. Going on to Cambridge, he entered Gonville and Caius College to read medicine, subsequently receiving his clinical training at Guy's Hospital. He qualified by taking the London Conjoint diploma in 1925. In the following year he obtained the degrees of M.B., B.Chir. Dr. Cuningham's first appointment was as paediatric house-physician in his own teaching hospital, and he followed on as resident obstetrician and gynaecologist. He then held posts in various capacities in the Brompton and Lambeth Hospitals until 1929, when, upon the untimely and sudden death of his father, he returned to Londonderry and took over the practice with the practically unanimous acceptance of all the patients. During the late 'thirties he became a medical officer in the Territorial Army. When the second world war began he volunteered for service abroad and served in the Middle East with the 9th (Londonderry) Heavy Anti-aircraft Regiment as its medical officer from 1939 to 1944. Afterwards he served in France and Belgium, where he was attached to the 8th Brigade's general hospital. He was mentioned in dispatches and ultimately attained the rank of major. After demobilization in 1945 he returned to his practice at Londonderry. From 1947 to 1952 he was honorary secretary of the Londonderry Division of the British Medical Association, becoming its chairman in 1952–3. He served also on the Northern Ireland Committee in 1953–4.

J. A. L. J. writes: "Ronnie," as he was affectionately known by his medical colleagues and friends, occupied a peculiar niche in the community which was all his own and which will be difficult to fill. Having fallen heir, so to speak, to a large mixed practice, he retained the affections of people of all creeds and classes in that practice to an extraordinary degree. His greatest flair was found in his innate kindliness, courtesy, and consideration for everybody, and everybody liked and admired him for it and deeply mourns his passing. Mention must also be made of his sterling professional qualities. He was a good, sound general practitioner in the very best tradition of the profession, and what better could be said of any man than that? He is survived by his wife and only son, John, who was serving with the Royal Ulster Rifles in Cyprus at the time of his father's death.

ARTHUR SCHÜLLER, M.D.

Professor Arthur Schüller, who died recently in Melbourne at the age of 83, was at one time professor of neurology and psychiatry at the University of Vienna. With Hand and Christian he was the first to describe the rare syndrome which is known eponymously by their names.

Arthur Schüller was born on December 28, 1874, at Brünn, in the area of the Austro-Hungarian Empire which is now part of Czechoslovakia. His father was a specialist in otolaryngology. He studied medicine at the University of Vienna, graduating M.D. in 1899 with special honours (*sub auspiciis imperatoris*), and at the early age of 36 he became professor of neurology and psychiatry at the University of Vienna.

Professor Schüller took refuge from Nazi oppression in Heidelberg, in the State of Victoria, a few miles from Melbourne. From 1940 onwards he worked in the *x*-ray department at St. Vincent's Hospital, Melbourne; and two years later he became honorary research officer in the anatomy department at the University of Melbourne. He obtained the degree of M.D. from two Australian universities, those of Sydney and Melbourne. Characteristically, in spite of the upheaval in his life, he continued to contribute articles on his specialty to medical journals: one paper on "*X*-ray Examination in Recent Head Injuries" was published in the *Medical Journal of Australia* in 1941, and another on "Cephalhaematoma Deformans" in *Surgery*, in 1946.

Dr. F. FRIEND writes: Professor Arthur Schüller died gently and happily as he had lived at the age of 83 in Melbourne. Dr. Keith Hallam, himself a leading radiologist, said about him that he was a world figure in the field of neurology. After his appointment to the professorial chair in Vienna, his main interest became *x*-ray diagnosis of the brain and skull. In 1905 he published his first book on the base of the skull, and later two more books about the radiology of the skull and the brain, together with innumerable papers. In 1893 Hand described defects in the skulls of children which are due to a lipoid disturbance of the reticulo-endothelial cells. Schüller described the radiological appearances of this rare disease, which is neither inherited nor due to race. Treatment can stop the progression of the disease after the first acute dangerous onset. Cure is possible. Diabetes insipidus and exophthalmos are combined with the disorder. Schüller pointed out that the defects resembled geographical maps—a characteristic of this disease.

Professor Schüller was an honorary member of many medical societies and a much-sought-after speaker at medical congresses. As a man he was gentle and unassuming. Students from all over the world came to him in Vienna. From 1905 onwards he had an *x*-ray plant in his consulting room, where he himself took films of the skull, which required a very long exposure at that time. In spite of the fact that this pioneer must have been exposed to a considerable degree of radiation, he attained the age of 83 without signs of radiation damage.

Professor Schüller is survived by his widow. His two sons were exterminated in a Nazi concentration camp.

DAVID McKAIL, M.D., F.R.F.P.S., D.P.H.

Dr. David McKail, for many years a well-known general practitioner in Glasgow, and one with a strong interest in preventive medicine, died at Harrow, Middlesex, on February 4. He was 83 years of age.

David McKail was born at Glasgow on August 22, 1874. From Dennistoun public school, where he was dux pupil in 1889, he went on to Allen Glen's School, where he gained a university bursary. At Glasgow University he had a successful career as a medical student, being junior Arnott prizeman and Joseph Black medallist, both in physics, and winning certificates of merit in several subjects. After graduating M.B., Ch.B., with commendation, in 1897, he worked for a time as a locumtenent and as an assistant before settling in practice in the Bridgeton district of Glasgow, in 1898. In 1907, the year in which he took the Cambridge D.P.H., the Glasgow Provincial Training College appointed him assistant lecturer in hygiene to student-teachers. Two years later he became a part-time school doctor under the Glasgow School Board and lecturer in forensic medicine and public health and director of the public health laboratory at St. Mungo's College, the medical school of the Glasgow Infirmary, where he was also lecturer in hygiene to trainee-nurses. His thesis for the M.D. degree, a study of the health of schoolchildren, was printed in the *Glasgow Medical Journal* in 1909. In the same year he was admitted a Fellow of the Royal Faculty of Physicians and Surgeons of Glasgow after examination in medicine and public health, and was elected an examiner for the D.P.H. of the Conjoint Board of Scotland. In 1913 the Faculty elected him examiner in forensic medicine and public health of candidates for the Scottish triple qualification. During the first world war he served with the R.A.M.C. at home and in France from 1915 to 1917, and, later, in hospital ships. In 1918 he was appointed sanitary administrative medical officer to the Admiralty Labour and Housing Department (Scotland), and for the next four years he served on pensions boards and as a medical referee. After the war he became a district medical officer under the Glasgow Parish Council and a factory surgeon for one of the Glasgow districts, holding the latter appointments until 1947, the year he retired. In 1922 he was appointed a member of the medical advisory committee under the Workmen's Compensation (Silicosis) Act, 1918. When he retired

at the age of 73 because of increasing deafness, the people of the east end of Glasgow made him a presentation.

Dr. McKail was an active member of the British Medical Association for forty years, and gave much of his time in its interests. He served on the Scottish Committee from 1923 to 1927; the Central Ethical Committee from 1929 to 1938; and the Charities Committee from 1936 to 1947. He was honorary secretary of the old Glasgow Eastern Division from 1922 to 1926, becoming its chairman in 1929, and chairman of the Glasgow Division in 1932–3. On twelve occasions he was a representative at the Annual Representative Meeting. When the B.M.A. held its Annual Meeting at Glasgow in 1922 he acted as one of the honorary secretaries of the Section of Medical Sociology, and at the Manchester Meeting in 1929 he served in a similar capacity for the Section of Occupational Diseases. At the Glasgow Meeting he opened a discussion before the Public Health Section on industrial fatigue and vocational selection. He was the author of *Public Health Chemistry and Bacteriology*, a book published in 1912. His wife died twenty-five years ago, and for some years past he had been living with a son-in-law in Pinner. He is survived by two married daughters and one son. His brother, Dr. T. J. McKail, is in medical practice in Glasgow.

T. LEVITT, F.R.C.S., F.R.C.S.Ed., F.R.C.S.I.

Mr. T. Levitt, formerly surgical assistant at the thyroid clinic, New End Hospital, Hampstead, died in Charing Cross Hospital on February 22, aged 49.

Tobias Levitt first studied medicine at Capetown, where he won first-class honours in anatomy and physiology. Coming to England, he continued his medical education at the Middlesex Hospital, qualifying by taking the Conjoint diploma in 1934. After working as demonstrator of anatomy at the Middlesex, Mr. Levitt was house-surgeon at Bedford County Hospital and Gloucester Royal Infirmary and surgical assistant medical officer at the Paddington General Hospital. In 1934 he took the F.R.C.S.I. During the second world war he served in the R.A.M.C. as a surgical specialist, and after the war he took the F.R.C.S. of Edinburgh in 1946 and the F.R.C.S. of England in 1948. As surgical first assistant at the thyroid clinic of the New End Hospital, Hampstead, he gained wide experience in the surgery of the thyroid gland. He wrote several papers on the subject and a book entitled *The Thyroid: a Physiological, Pathological, Clinical, and Surgical Study*. An excellent and inspiring teacher, he was lecturer in surgery to the Fellowship of Postgraduate Medicine at the New End Hospital for a number of years.

W. W. D. writes: "Toby" Levitt was probably the only person who obtained all three surgical Fellowships by examination in the days before the primary was "reciprocal." Perhaps it was this experience that enabled him to understand so well postgraduates who were striving to pass the final F.R.C.S. He will be remembered all over the Commonwealth, and particularly in India, for the endless trouble he took with these students. He poured out his life's blood for them. Many who had abandoned hope of ever passing the examination found new hope with him. The various details and hazards of the Fellowship were rehearsed continuously—what to wear, how to stand, how to speak—no detail was too much for him. When the great day came many candidates found the examination an anticlimax, having attended his course in the wards of New End Hospital. Generous of heart, he often refused financial reward for his teaching. For a long time he was associated with Sir Geoffrey Keynes and Mr. J. E. Piercy as first assistant at the New End thyroid clinic. The knowledge gained there culminated in his election to a Hunterian Professorship in 1952. The lecture he gave held his audience spellbound and will long be remembered as a model of its kind. Following this, his book, *The Thyroid*, was published in 1954. This large volume provoked world-wide discussion. Produced with the same scrupulous care which characterized his teaching, its concepts, although unacceptable to many, were most stimulating and thought-provoking and led to advance in the subject.

Early in 1952 he had his first attack of coronary thrombosis, and this was to return again during an extensive lecture tour in the United States and during his final illness. He was attached to the Royal Marsden Hospital in a research capacity and was at work on a book on carcinoma and the thyroid when his intense life came to an end.

> "Before my pen has glean'd my teeming brain,
> Before high piled books on charact'ry
> Hold like rich garners the full ripen'd grain."

He is lamented by many.

J. W. MALIM, M.B., B.Chir.

Dr. J. W. Malim, who was in general practice at Torquay for many years, died at his home at St. Marychurch, on February 6, aged 81.

Jeffrey Wentworth Malim was born on January 29, 1877, the son of the Rev. W. G. Malim. From Christ's College, Cambridge, where he gained a second-class pass in Part 1 of the Natural Sciences Tripos, he then went on to St. Bartholomew's Hospital, and graduated M.B., B.Chir., in 1900. During the next few years he held resident appointments at the Bristol General Hospital, the Liverpool Stanley Hospital, and the Royal Mineral Water Hospital, Bath. He then served as a ship surgeon for a time before entering general practice at Harrogate, where he became honorary anaesthetist to the infirmary. At the outbreak of the first world war he joined the R.A.M.C. and served in France and Ireland. After demobilization he paid a long visit to Jamaica and South Carolina, where he was in practice for a time, before returning to England to settle in Torquay in 1922. He became an authority on Dartmoor, being the author of a book on that subject, and of another on Bodmin Moor. His first wife, Mary Hadley, whom he met as a nurse at Bristol General Hospital, died in 1953. He is survived by his second wife, formerly Florence Emily Hardwick, and by two sons of the first marriage, one of whom is in medical practice at Torquay and the other is a solicitor in the same town.

BEDRICH WINTER, M.D.

Dr. Bedrich Winter died suddenly at his home at Bourn, Cambridgeshire, on February 4 at the age of 68.

Bedrich Winter was born at Prague on August 22, 1889, and was educated at the university there, graduating M.D. in 1913. After further study at the Prague and Munich Universities he established himself as a gynaecologist at Augsburg, where he was soon counted among the foremost specialists. At an early stage of the changed regime he left Germany and returned to his native Prague. Even there his stay was comparatively short, and towards the end of 1939 he came to England. At that time he spoke only a few words of English, so that on his arrival in this country, and at the age of 50, he had to study very hard to prepare himself for a new future. After holding various hospital appointments he settled in the Caxton district of Cambridgeshire, first as an assistant and later as a partner to Dr. E. P. H. Dudley. After the death of his partner he moved to Bourn, and became the partner of Dr. T. Meurig Owen. His knowledge, his powers of quick and sure diagnosis, the personal touch he coupled with medical treatment, and his untiring efforts in serious cases soon paved the way to close ties between his patients and himself. It was by their confidence, regard, and friendship that his patients recompensed him for what he did for them, and it was this trust which was his greatest joy and satisfaction during the last years of his life.

H. O. M. MEREWETHER, O.B.E., F.R.C.S.Ed.

Professor W. I. C. MORRIS writes: The obituary of Mr. H. O. M. Merewether in your issue of February 1 (p. 285) was the first intimation I had had of a death which many will mourn. While it pays tribute to Merewether's achievements at the crown and close of his career, it is less eloquent on Merewether in his youth, as I, for one, shall always remember him. He was one of a group of students from Commonwealth countries who added greatly to the gaiety of undergraduate life in Edinburgh in the late 'twenties. He was somewhat older than the home-bred students, a tall man, of magnificent physique, his neat, shapely head set on manly shoulders, his back erect, his stride that of the fine athlete which he was, filled with grace and energy. With these qualities he combined an astringent wit and a maturity of comment which made him a strong educative influence in student society. It is many years since I met him, but our Christmas card exchanges were always accompanied by some vibrant message from him couched in terms of affection tinged with the kindliest mockery, for which all who knew him valued him. He worked hard. He played hard. We are the richer for knowing him.

M. D. SHEPPARD, M.B., F.R.C.S.

The obituary of Mr. M. D. Sheppard was printed in the *Journal* of February 15 (p. 404).

W. L. N. writes: May I add a line about my old friend, M. D. Sheppard, who sat with me through most of our time in medical school at U.C.H.? He was one of the most indefatigable workers I have met. I remember how when he was working (successfully) for his primary Fellowship he would repair a car he had bought second-hand in the Euston Road. His diagnostic skill in the purchase of this car—which was found to have a broken pinion in the gear-box—was not of the same standard as in surgery, but his operative skill at repairing it was. He would work on the car till 1 a.m., and then settle down to his anatomy and physiology, and to cap it was the first to be in his seat for next morning's nine-o'clock lecture. A year ago when I was in Chelmsford I inquired if he had retained his zest for operating, and was greeted with laughter, as apparently the length of his operating session was notorious. He was a delightful man, and in every way his death is a great loss.

Medico-Legal

LIFE SENTENCE FOR "DIMINISHED RESPONSIBILITY" MANSLAUGHTER

[FROM OUR LEGAL CORRESPONDENT]

On January 29[1] Cebert Bastian, aged 32, was found guilty of the manslaughter of his two sons aged 4 and 3. He was charged with murder, but the jury rejected the prosecution's submission that their verdict should be guilty but insane and upheld the defence of diminished responsibility.

When Bastian was arraigned he at first pleaded guilty, but when in answer to Mr. Justice Donovan he said he did not altogether remember what had happened a plea of not guilty was entered. Bastian, who suffered from tuberculosis, stayed at home looking after the children while his wife went out to daily jobs. When he gave himself up at the police station he said he had murdered his two children by hitting them with a rolling-pin. All three doctors who gave evidence agreed in the opinion that at the time Bastian did not know that what he was doing was wrong. Dr. F. H. Brisby, principal medical officer at Brixton, thought that he did not even know what he was doing.

In sentencing Bastian to life imprisonment the judge said that the medical evidence made it clear that a short term of imprisonment would not be a proper penalty, but that if Bastian recovered the authorities would be in a position to release him. So in the result there is not much difference for Bastian in having been found guilty of manslaughter instead of guilty of murder but insane.

[1] *Manchester Guardian*, January 30.

DAMAGES FOR LOSS OF EXPECTATION OF LIFE

[FROM OUR LEGAL CORRESPONDENT]

The common law rule used to be that a person's cause of action for a tort—for example, for damages for personal injuries caused by negligence—died with him. The Law Reform (Miscellaneous Provisions) Act, 1934, however, provided that with certain exceptions a cause of action in tort vested in someone at his death should survive for the benefit of his estate and be maintainable by his executors. As a consequence many claims were brought by the executors of people killed in road and industrial accidents, and among the heads of damage claimed was loss of expectation of life. In 1937 the House of Lords[1] confirmed that such a head of damage was recoverable. In 1938[2] it was held that, even though death was instantaneous, the cause of action had nevertheless vested in the deceased and could be litigated by his executors. As was to be expected, widely varying sums, often very large, were awarded, until in 1941 the House of Lords put its foot down. In the case of *Benham v. Gambling*[3] a child aged 2½ was killed in an accident, and for its loss of expectation of life £1,200, a figure then regarded as average, had been awarded.

The House of Lords reduced this figure to a mere £200, saying that it was not the length of life lost but the loss of prospective happiness which had to be assessed. Their Lordships recognized that this was really incapable of being measured in coin of the realm at all, and the standard which they then set has resulted in awards so modest as to have become merely conventional ever since, especially in view of the impact of inflation since 1941. On January 30 last, however, the Court of Appeal[4] contrived to escape the rigour of the *Benham v. Gambling* decision in the circumstances before them.

Mr. Norman Davies, of Lordswood, Southampton, had been awarded £16,500 damages, including £1,500 special damage, for personal injuries sustained in a road accident. Mr. Davies was 56 years of age. Immediately after the accident he had made a substantial recovery, but before the trial his condition had seriously deteriorated, he was living a life of increasing pain and could no longer sleep at night, and it appeared from the medical reports that he could expect to live only five more years at most. The defendant appealed on the ground that, as Mr. Davies's loss of prospective net earnings could fairly be assessed at £2,500, the balance of £12,500 was a grossly excessive award for pain and suffering, considering that by reason of the rule in *Benham v. Gambling* only a few hundred pounds of that balance were attributable to loss of expectation of life.

In his judgment the Lord Chief Justice said that as far as loss of expectation of life was concerned the court was bound by the decision in *Benham v. Gambling*. There was no distinction between an action brought by the injured person and an action brought by his executors when he had not survived. But even though Mr. Davies was not entitled to a substantial award under this head, he had a claim for pain and suffering which would be swelled by the mental agony of knowing that the days of life left to him were fewer and would be spent in pain, suffering, and misery.

The court could not say that the award of £16,500 was a wholly erroneous estimate of what should have been awarded, and the appeal was therefore dismissed.

As the Lord Chief Justice observed during the argument, it has always been thought cheaper to kill than to injure.

[1] *Rose* v. *Ford* [1937] A.C. 826.
[2] *Morgan* v. *Scoulding* [1938] 1 K.B. 786.
[3] [1941] A.C. 157.
[4] *The Times*, January 31.

Medical Notes in Parliament

LAW ON MENTAL ILLNESS AND MENTAL DEFICIENCY

The EARL OF FEVERSHAM, chairman of the National Association for Mental Health, called the attention of the House of Lords on February 19 to the implications of the recommendations of the Royal Commission on the Law relating to Mental Illness and Mental Deficiency, which he described as one of the outstanding social documents of the century. He championed the belief that the greatest requirement for the well-being of society in the modern age was that each individual should have complete integration of body, mind, and spirit. Speed, mobility, and diversity had imposed many new strains. To-day it was infinitely more difficult to have a balanced personality and stability of mind than ever before. Some thinking people said that the only hope of survival was for man to devote greater resources to discovering more about himself and his mind, and to learn more about the factors that impelled him through emotional or irrational motives to act as he did. The keynote of the report was the emphasis on treatment, as distinct from custodial care. The main objects of the changes were to put mental patients, so far as possible, on the same footing as patients in other hospitals.

Responsibility of Local Authorities

The most far-reaching recommendation was that the responsibility for community care should be placed firmly on the local authorities. Superintendents of mental hospitals told him that if that was put into effect about 20,000 long-stay patients could be discharged—people who no longer benefited from skilled nursing and could leave hospital provided they had a good home to go to or a hostel run by the local authority. But it was useless to postulate the importance of prevention and aftercare, and to allow thousands of patients to be discharged, unless the local authorities were able, and prepared with trained workers, to accept the burden that would fall on them. It was imperative that families who would be asked to take patients back into their homes should have the help and advice of people specializing in this field. Unless the status of the mental health service was improved the patients discharged would be back inside the hospital within a few weeks, and the chaos to the community would be unthinkable.

Mental welfare services would not be improved unless money was made available. The whole question hinged on finance. Even in these days of financial stringency the Government must devise some method of giving local authorities a financial incentive. The paucity of research in mental health was scandalous: only £58,000 of public money was being spent on it this year. There would not be progress until the State made a determined effort to promote the discovery of new knowledge of the mind. A permanent foundation was needed, investigating the normal behaviour of the human mind and the effect of various influences upon it.

Lord PAKENHAM, referring to the unwilling patient, suggested that the proposed period of one year detention was too long, and an initial period of six months preferable, with a mental health tribunal review if the doctor thought further treatment under detention advisable. There was no criticism of the "mentally ill patients" group to cover the disorders of a normally developed mind. But there was a good deal of criticism of the other two suggested groups—psychopathic patients, and severely subnormal patients. There was some doubt whether it was practical or clinically permissible to include "patients at present classified as feeble-minded" in the psychopathic group. Surely it was better to recognize a psychopathic group reserved for abnormal personalities with anti-social tendencies, and to reserve the third group for subnormal personalities, including the high-grade and the feeble-minded. Those three groups—the mentally ill, the psychopathic group with normally developed minds, and the subnormal—would be a better classification than the one suggested by the Royal Commission.

Changed Medical Outlook

Lord COHEN OF BIRKENHEAD said that in the past 25 years there had been an increasing recognition of the physical factors which contributed to mental disease, and a reorientation of the medical outlook. In place of custodial care for the benefit of society, attention had been directed to the clinical needs of the individual patient: mental institutions had become mental hospitals in fact, and not simply in name. Emphasizing the magnitude of the problem, he said that one in 250 of the population occupied a bed in a mental hospital; one child in 10 would suffer from some form of nervous breakdown; and one child in 100 was within the definition of mentally defective. Illustrative of the change in public opinion towards the mentally afflicted was the fact that in 1946 there were about 35,500 admissions to mental hospitals, and in 1956 there were 88,000, of whom 75% were voluntary. The amount of research was not to be measured simply by the fact that last year only about £58,000 out of £2,689,000 spent by the Medical Research Council was devoted to research on mental disease. Quite a lot was being spent in neurology, anatomy, physiology, and so forth, which might have their bearing on the elucidation of mental health problems. In genetics, and even in biology, many advances were being made. There were also other organizations—for example, the Nuffield Provincial Hospitals Trust, which was responsible for the Worthing experiment on the day hospital service—concerned with mental health research. What was lacking was, to a large extent, ideas and men. New "thinking caps" were needed, and new research into the fundamental sciences; a chance observation in one of them might provide the key to the mysteries of some mental health problems.

Government Reply

The LORD CHANCELLOR said the underlying principle of the report was that people suffering from mental illness or disability should be treated so far as possible on the same footing as other sick or disabled people. The Royal Commission's recommendation that the assumption should be abandoned that procedures authorizing compulsory detention must be used unless a patient could express a positive desire for treatment would mean that patients could be admitted to mental or mental deficiency hospitals with no more formality than when entering any other hospital. It had been widely welcomed, and the Government had been advised that it could be applied to mental defectives within the terms of the present law. For these patients the Minister of Health had already asked hospitals and local authorities to regard completely informal admission as the normal method in future. Hospitals had also been asked to review their present patients and to recommend the discharge of the order of detention in all cases in which the patient could suitably remain in hospital on an informal basis. Completely informal admission for the mentally ill—as distinct from mental deficiency hospitals—would not be possible without a change in the law. Informal admission to the mental deficiency hospitals was the only one of the Royal Commission's major recomendations on procedures that could be put into effect without an alteration in the law.

The Government accepted the need for new legislation to replace the Lunacy and Mental Treatment Acts and the Mental Deficiency Acts, and that it should be broadly on the lines recommended by the Royal Commission, subject to a few modifications that were considered desirable in the light of views expressed since the publication of the report. He could not say when such legislation could be introduced, but in his opinion it would be a major piece of legislation.

The terms proposed by the Royal Commission to define categories of patients had aroused considerable differences

of opinion. "Psychopath" in the wide sense the Commission proposed had been a stumbling-block for many who disliked the idea of using one term to cover not only aggressive anti-social psychopaths but also patients with limited intelligence who were normally well behaved. There had also been some criticism of the term "severely abnormal." The Government recognized that careful consideration must be given to the categories of patients and the question of definitions, and he would devote a great deal more thought to the names and the definitions, and to how far they should go in the legislation.

On the work of local authorities, the Government fully accepted the principle underlying the Commission's recommendations, but it must also take into account the general economic and financial situation and the proposed introduction of a general grant instead of a percentage grant for specific local authority services. It wished to see development on the lines recommended by the Commission to the fullest extent practicable, and intended to invite the local authority associations to discussions. Local health authorities at present employed about 30 psychiatric social workers and about 1,000 mental welfare officers. The shortage of psychiatric social workers was due mainly to the limited number of men and women who had the necessary aptitude and suitability for the university course. It was hoped that more would be obtained, and that it would become increasingly common for them to work jointly for the local authorities and for the hospitals in the same locality. The Government was conscious of and grateful for the steady, unspectacular, but important work of the mental welfare officers. The terms of reference to the Younghusband Committee on the recruitment and training of social workers included mental welfare officers, and decisions on their future training should await the report of the committee.

Tax on Joint Incomes

Mrs. LENA JEGER (Holborn and St. Pancras South, Lab.) asked the Chancellor of the Exchequer how much income tax would have to be paid by two unmarried doctors living together with a gross joint income of £4,000; and how much would be payable by two married doctors, presuming the expenses to be identical.

Mr. J. E. SIMON, Financial Secretary, Treasury, replying on February 20, said that, assuming that the income was all earned and that there were no dependants, the income tax and surtax payable would be between £1,083 and £1,490 in the case of two single persons, and between £1,310 and £1,430 in the case of a married couple, depending on the amount earned by each person.

Mr. Simon also informed Mrs. Jeger that about 85,000 working wives paid surtax on the whole of their income, taking the wife's earned income as the top slice of the joint income. The cost of abolishing aggregation would be nearly £5m. in a full year, on the assumption that the separation applied only to earned income.

Mrs. JEGER commented on both replies that they indicated an unfair incidence of taxation and surtax.

Poliomyelitis Vaccine

Sir ALFRED BOSSOM (Maidstone, Con.) asked the Minister of Health if he would give consideration to increasing the imports of Salk vaccine against poliomyelitis to supplement British vaccine and ensure that a more adequate amount was available to protect children, as considerable anxiety was felt at the small quantities at present being imported compared with the need. Mr. D. WALKER-SMITH stated on February 21 that substantial quantities of Salk vaccine were already being imported to supplement supplies of British vaccine, and he was satisfied that good progress was now being made with the vaccination programme. He was keeping the position under constant review.

Mr. S. P. VIANT (Willesden, West, Lab.) asked the Minister what recommendations regarding the necessity for a third injection with poliomyelitis vaccine he received from the advisory committee of doctors who considered this matter in December; and what decision he had arrived at. Mr. WALKER-SMITH stated that the advice he had had was to the effect that first priority should be given to increasing the number of persons in the particularly susceptible groups who were vaccinated with two injections. The position would be kept under review, but for the time being he was continuing to concentrate on this.

Prescription Costs in Scotland

Mr. J. NIXON BROWNE, Under Secretary, Scottish Office, informed Dr. DICKSON MABON (Greenock, Lab.) on February 18 that in the first eight months of 1957 the aggregate number of Health Service prescriptions dispensed in Scotland was 13,200,000, compared with 14,400,000 in the corresponding period in 1956. The average total cost was 81.04 pence, compared with 67.8 pence in 1956; and the net cost after deducting charges payable by patients was 68.26d. in 1957 and 58.84d. in 1956.

Vital Statistics

Week Ending February 15

The largest changes in the returns of the notifications of infectious diseases in England and Wales during the week ending February 15 were increases of 745 for measles, from 3,752 to 4,497, 267 for dysentery, from 1,060 to 1,327, and 17 for scarlet fever, from 871 to 888; the largest decreases were 145 for whooping-cough, from 721 to 576, and 141 for acute pneumonia, from 1,023 to 882.

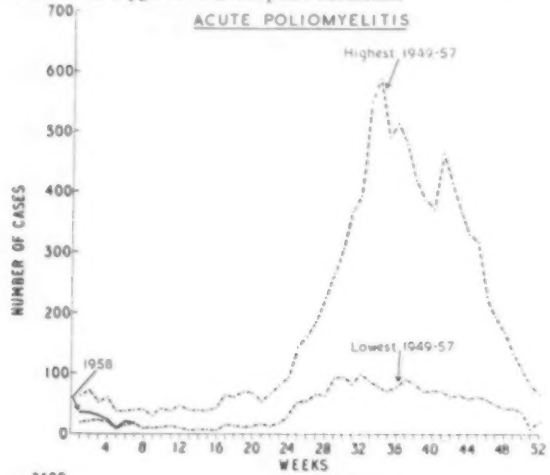
The increase in the incidence of measles was largest in the south-eastern counties and Wales. The largest rises were 158 in Surrey, from 62 to 220 (Malden and Coombe M.B. 55, Merton and Morden U.D. 55), 80 in Southampton County, from 278 to 358 (Portsmouth C.B. 93, Southampton C.B. 81), 55 in Carmarthenshire, from 73 to 128 (Llanelly R.D. 55, Llanelly M.B. 41), and 50 in Kent, from 129 to 179 (Bromley M.B. 80); the largest falls were 56 in Devonshire, from 188 to 132, and 56 in Yorkshire North Riding, from 225 to 169. The largest rise in the number of notifications of scarlet fever was 35 in Essex, from 58 to 93. The incidence of whooping-cough decreased in most regions of the country, but there were no large local fluctuations. Three cases of diphtheria were notified, being the same number as in the preceding week. A fall in the number of notifications of acute pneumonia was recorded throughout the country; the largest was 61 in London, from 123 to 62.

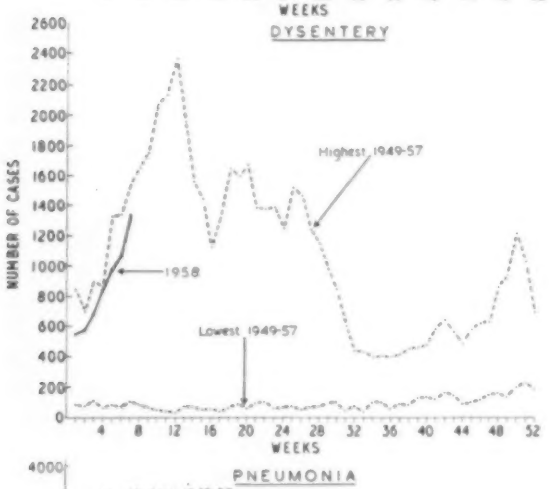
The notifications of acute poliomyelitis numbered 18, and these were 3 fewer for paralytic and 1 more for non-paralytic cases than in the preceding week. The largest returns were Cornwall 3 (Penzance M.B. 2), Kent 3, Yorkshire West Riding 3.

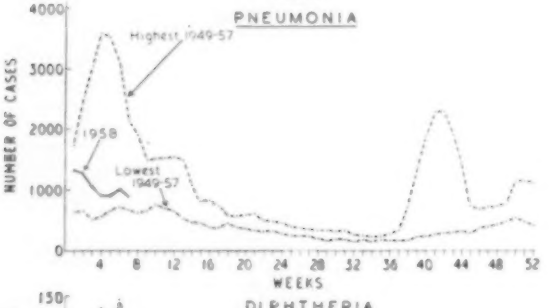
A rise in the incidence of dysentery occurred in most of the established outbreaks; the largest was 148 in Lancashire. The chief centres of infection were Lancashire 479 (Oldham C.B. 124, Middleton M.B. 64, Liverpool C.B. 55, Chadderton U.D. 53, Manchester C.B. 36, St. Helens C.B. 36, Eccles M.B. 15, Bolton C.B. 13, Salford C.B. 13, Failsworth U.D. 13), London 203 (Finsbury 45, Islington 36, Southwark 25, Fulham 22, Stoke Newington 19, Bethnal Green 10), Yorkshire West Riding 202 (Sheffield C.B. 79, Thorne R.D. 21, Leeds C.B. 20, Dewsbury C.B. 15, Huddersfield C.B. 12, Saddleworth U.D. 10), Durham 54 (South Shields C.B. 14, Whickham U.D. 13); Warwickshire 40 (Birmingham C.B. 30), Middlesex 38 (Ruislip-Northwood U.D. 12), Caernarvonshire 35 (Bangor M.B. 24, Pwllheli M.B. 10), Southampton County 32 (Portsmouth C.B. 25), Yorkshire North Riding 32 (Middlesbrough C.B. 16), Staffordshire 29 (Newcastle under Lyme M.B. 20), Nottinghamshire 26, Yorkshire East Riding 20 (Haltemprice M.B. 11).

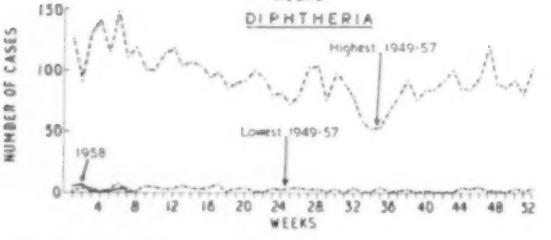
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the years 1949–57 are shown thus - - - - - -, the figures for 1958 thus ————. Except for the curves showing notifications in 1958, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **February 8** (No. 6) and corresponding week 1957.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the whole of England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	3	0	4	0	4	9	2	1	0	2
Dysentery	1,060	182	196	13	2	1,290	67	213	7	1
Encephalitis, acute	3	0		0		5	1		0	
Enteric fever:										
Typhoid	2	0	0	0	12 (B)	6	1	0	0	
Paratyphoid	2	0	0	0		5	0	2 (B)	0	
Food-poisoning	163	15	70	0		165	31	60	1	
Infective enteritis or diarrhoea under 2 years				6	29				16	28
Measles *	3,752	64	94	26	16	16,752	1353	504	505	301
Meningococcal infection	37	6	13	0		28	2	10	3	1
Ophthalmia neonatorum	26	0	7	0		29	2	7	0	
Pneumonia †	1,023	123	374	22	5	720	58	270	59	2
Poliomyelitis, acute:										
Paralytic	16	0	2	0	3	21	5	3	1	9
Non-paralytic	4	0				13	3			
Puerperal fever §	243	58	10	0		222	45	9	0	1
Scarlet fever	871	67	68	23	24	869	62	74	35	26
Tuberculosis:										
Respiratory	599	64	105	16		666	86	121	16	
Non-respiratory	68	5	13	5		75	6	21	5	
Whooping-cough	721	38	26	5	21	3,148	164	423	14	44

DEATHS	1958					1957				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	1	No comparable figures available.	0	0	0	0
Dysentery	2	0	0	0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0			0	0	0	
Infective enteritis or diarrhoea under 2 years	8	0	0	0	3		0	0	0	0
Influenza	184	13	2	0	2		2	1	0	0
Measles		0	0	0	0		0	0	0	0
Meningococcal infection		0	2				0	0		
Pneumonia	891	81	42	25	8		43	20	11	12
Poliomyelitis, acute	2	0		0	0		0			0
Scarlet fever		0	0	0	0		0	0	0	0
Tuberculosis:										
Respiratory	121	11	14	2	2		6	10	2	0
Non-respiratory		1	1	0	1		2	0	0	1
Whooping-cough	1	0	0	0	0		0	0	0	0
Deaths 0–1 year	390	28	33	9	20		38	19	10	9
Deaths (excluding stillbirths)	12,631	976	717	155	221		786	653	128	180
LIVE BIRTHS	14,283	1151	954	221	393		1213	1031	245	368
STILLBIRTHS	350	29	34				23	17		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

B.M.A. Film Competition.—The winners of the B.M.A.'s 1957 competition for 16-mm. medical films were:—*Non-Commercial Category:* First prize, "Treatment of Paraplegia due to Fracture-dislocation of Dorso-lumbar Spine" (black and white, sound, 45 min.), Mr. F. W. HOLDSWORTH, F.R.C.S., and the department of medical photography, United Sheffield Hospitals; awards of merit, "A Method of Corneal Grafting" (colour, silent, 15 min.), Mr. A. G. LEIGH, F.R.C.S., and the medical illustration department, Institute of Ophthalmology, London, and "Rehabilitation of Double Leg Amputee" (colour, silent, 13 min.), management committee and department of medical photography of the Southend-on-Sea Hospital. *Commercial Category:* First prize, "The Human Blood Fluke" (colour, sound, 33 min.), Wellcome Laboratories of Tropical Medicine and Wellcome Film Unit; awards of merit, "The Conjoined Twins of Kano" (colour, sound, 39 min.), Professor IAN AIRD, F.R.C.S., and Stanley Schofield Productions, Ltd., and "The Jugular Venous Pulse" (colour, sound, 20 min.), Dr. PAUL WOOD and Wellcome Film Unit. "One Man's Challenge" (black and white, sound, 20 min.), Dr. G. R. FEARNLEY (British Empire Rheumatism Council) and Derek Stewart Productions for Lloyd-Hamol, Ltd., was awarded a special commendation for a film judged not to be a medical film for the purposes of the competition. Details of the Association's 1958 medical film competition will be announced shortly.

Research on Cardiovascular Function and Disease.—Details of the grants-in-aid to institutions and research fellowships offered by the Life Insurance Medical Research Fund of Australia and New Zealand may be obtained from the Fund's medical director, 87, Pitt Street, Sydney, New South Wales. The Fund, which was established by the Life Offices' Association for Australasia, at present limits its support to research in the field of cardiovascular function and disease. Applications for grants or fellowships must be received by July 1.

Medical and Dental Defence Union of Scotland.—The Union held its 55th annual meeting on February 21 in Glasgow. Membership at the end of the year (August 8, 1957) stood at 8,443, and the amount paid in damages during the year was £869. In the annual report it is noted that the number of complaints by patients to executive councils about doctors and dentists has continued to fall. The Union's council draws attention to the "increasing habit" of some consultants when reporting to general practitioners on their patients to send such reports either signed by a secretary or marked "Dictated but not read." The council considers this undesirable and potentially dangerous to patients.

Journal on Health Education.—The International Union for Health Education, a non-governmental organization founded in 1951, has started an official quarterly journal, *International Journal of Health Education*. The first issue appeared in January. The journal is published in French and English and is obtainable (price 20s. per annum) from the editorial office, 3, rue Viollier, Geneva. The publishers are Studer S.A., of Geneva. Dr. JOHN BURTON, medical director of the Central Council for Health Education, is one of the journal's editorial committee of five; he is also named as the national correspondent for Great Britain.

Local Government in Greater London.—The Royal Commission on Local Government in Greater London has written to local authorities in the area inviting them to submit evidence. The Commission is also prepared to receive evidence from members of the public. Any person who wishes to do so should send his evidence in writing to the secretary of the Commission (Mr. J. R. Niven) at Sanctuary Buildings, 16, Great Smith Street, London, S.W.1.

Professor W. Hobson has resigned his chair as professor of social and industrial medicine at Sheffield on his appointment as medical officer for training and education at the W.H.O. regional office for Europe in Copenhagen.

Dr. J. H. Sheldon.—The general purposes committee of the Wolverhampton Town Council has recommended that the honorary freedom of the borough should be conferred on Dr. J. H. SHELDON, senior physician of the Royal Hospital, Wolverhampton, and widely known for his pioneer work for the care of the elderly.

COMING EVENTS

Hugh Cairns Memorial Lecture.—This lecture, details of which we announced last week (February 22, p. 473), has been postponed.

D.M.R.D. and D.M.R.T.—Courses for candidates for the D.M.R.D. and D.M.R.T. (R.C.P.Lond., R.C.S.Eng.) starting next October are now being organized by the Faculty of Radiologists. Further information is given in our advertisement pages.

Joseph Clover Lecture.—Professor W. D. M. PATON, F.R.S., will lecture on "Mechanisms of Transmission in the Central Nervous System" at 4 p.m. on March 19, at the Royal College of Surgeons, Lincoln's Inn Fields.

Grey Turner Surgical Club.—Meeting at Glasgow, March 24–26. Details from Mr. GORDON N. BAILEY, F.R.C.S., 2a, Lancaster Road, Harrogate.

Society of Apothecaries.—Course of 12 lectures in advanced surgery, suitable for candidates for the final F.R.C.S., on March 27, 28, and 31, and April 1, 2, and 3, at the Society's Hall, Blackfriars Lane, London, E.C.4 (fee £5 5s.). Further details from the registrar of the society.

Lister Oration.—Sir STEWART DUKE-ELDER will lecture on "The Emergence of Vision in the Animal World" at 4.30 p.m. on March 28, at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C.2.

British Occupational Hygiene Society.—Conference on "Noise" (particularly noise in industry), April 1, in London. Details from Dr. D. TURNER, the Associated Ethyl Company Limited, Ellesmere Port, Cheshire.

Institute of Diseases of the Chest.—Week-end course for general practitioners, April 19 and 20. Details from the dean of the institute, Brompton, London, S.W.3.

Fifth International Congress of Internal Medicine.—April 24–26, in Philadelphia. Details from the congress's secretary-general, Mr. E. R. LOVELAND, 4200, Pine Street, Philadelphia, 4, Pennsylvania.

NEW ISSUES

SPECIALIST JOURNALS AND ABSTRACTS

The journals listed below are obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

Journal of Neurology, Neurosurgery, and Psychiatry.—Issued quarterly (£3 annually). The new issue, Vol. 21, No. 1, includes:

THE RELATIVE MERITS OF ENCEPHALOGRAPHY AND VENTRICULOGRAPHY FOR THE INVESTIGATION OF INTRACRANIAL TUMOURS. Gösta Norlén and Inemar Wickbom.

ISCHAEMIC AND POST-ISCHAEMIC NUMBNESS AND PARAESTHESIAE. P. W. Nathan.

THE SURGICAL PROGNOSTIC SIGNIFICANCE OF THE ELECTROENCEPHALOGRAPHIC PREDICTION OF AMMON'S HORN SCLEROSIS IN EPILEPTICS. W. A. Kennedy and Denis Hill.

A REPORT OF TWO CASES OF THE JUVENILE FORM OF AMAUROTIC FAMILIAL IDIOCY (CEREBROMACULAR DEGENERATION). Michael Jefferson and M. L. Rutter.

SPINAL ANGIOMA WITH SYMPTOMS IN PREGNANCY. M. J. D. Newman.

PULSATING EXOPHTHALMOS IN VON RECKLINGHAUSEN'S DISEASE. Charles Lanzmaid and Alex Daws.

OPTIC ATROPHY AND NERVE DEAFNESS IN DIABETES MELLITUS. D. A. Shaw and L. J. P. Duncan.

SODIUM AMYTAL AND EXTRAVERSION. S. G. Laverty.

A CONTROLLED TRIAL OF METHYL PHENIDATE (RITALIN) IN THE TREATMENT OF DEPRESSIVE STATES. A. A. Robin and S. Wiseberg.

EPINEPHRINE METABOLITES AND PIGMENTATION IN THE CENTRAL NERVOUS SYSTEM IN A CASE OF PHENYLPYRUVIC OLIGOPHRENIA. J. H. Fellman.

PROCEEDINGS OF THE SOCIETY OF BRITISH NEUROLOGICAL SURGEONS: 56TH MEETING.

Journal of Clinical Pathology.—Issued six times a year (£4 4s. annually). The new issue, Vol. 11, No. 1, includes:

THE HISTOGENESIS OF PRIMARY HEPATIC CARCINOMA. I. P. Beswick and G. B. D. Scott.
PRIMARY LIVER CELL CARCINOMA 24 YEARS AFTER INTRAVENOUS INJECTION OF THOROTRAST. A. D. Morgan, W. H. W. Jayne, and D. Marrack.
FOAM CELLS IN THE STROMA OF CARCINOMA OF THE BODY OF THE UTERUS AND UTERINE CERVICAL POLYPI. Hilda R. Harris.
NON-SILICIOUS, DOUBLY REFRACTILE CRYSTALS IN THE GIANT CELLS OF TUBERCULOSIS. Charles P. Farthing and Basil G. Pickles.
FAT EMBOLISM STUDIED IN 100 PATIENTS DYING AFTER INJURY. H. E. Emson.
TRAUMATIC DISSECTING ANEURYSMS. T. K. Marshall.
ANTITHROMBOPLASTIN: THE DEGENERATION OF INTRINSIC THROMBOPLASTIN IN NORMAL SERUM. C. G. Berry.
PLACENTAL TRANSFER OF THE LUPUS ERYTHEMATOSUS FACTOR. David Burman and R. A. M. Oliver.
A LEUKAEMOID BLOOD PICTURE IN MEGALOBLASTIC ANAEMIA OF THE PUERPERIUM. G. Sclare and J. Cragg.
RH ANTIBODIES AND THE PROZONE PHENOMENON. P. H. Renton and Jeanne A. Hancock.
THE INFLUENCE OF AGE ON RED CELL DIAMETER. A. I. Spriggs and R. A. Sladden.
COMPARISON OF QUICK'S, OWREN'S, AND WARE'S TECHNIQUES FOR THE CONTROL OF ANTICOAGULANT THERAPY. M. Toohey.
OWREN'S METHOD FOR THE CONTROL OF ANTICOAGULANT THERAPY. M. J. Allington.
THE ISOLATION OF CHROMOGENIC MYCOBACTERIA FROM LARYNGEAL CULTURES. Miklós Lányi.
A METHOD FOR TYPING SHIGELLA SONNEI, USING COLICINE PRODUCTION AS A MARKER. J. D. Abbott and R. Shannon.
THE RESPONSE OF URINARY 17-HYDROXYCORTICOIDS TO CORTICOTROPHIN ZINC AS A TEST OF ADRENAL CORTICAL FUNCTION. J. S. Jenkins.
STUDIES ON FIBRINOLYSIN USING A CLINICALLY PRACTICAL METHOD OF QUANTITATIVE DETERMINATION. Edward Adelson and William H. Roeder.
A COMMENT ON THE FRACTIONAL INDIRECT DIAZO REACTION. F. Vella.

Abstracts of World Medicine.—Issued in the first week of each month, this journal contains abstracts of important papers selected from the current medical literature of the world. Annual subscription £4 4s.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ● Application should be made first to the institution concerned.

Sunday, March 2

COLLEGE OF GENERAL PRACTITIONERS: WELSH FACULTY.—At Lecture Theatre, Maternity Hospital, Cardiff Royal Infirmary, 11 a.m., Professor M. Essex: Diagnosis and Treatment of Emotional Problems in Children.

Monday, March 3

POSTGRADUATE MEDICAL SCHOOL OF LONDON.—4 p.m., films, Dr. P. Hugh-Jones: Mechanical Ventilation in Respiratory Disease; Bronchoscopy.

Tuesday, March 4

B.B.C. TELEVISION.—9.30 p.m., "Your Life in Their Hands," No. 4.—Out on a Limb, from Stratton, near Bude, Cornwall.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Mr. A. T. Gray: Cosmetic Materials.
INSTITUTE OF NEUROLOGY.—5.30 p.m., Professor N. F. Maclagan: Biochemistry of Coma.
LONDON HOSPITAL.—8 for 8.30 p.m., Professor Clifford Wilson: The Kidney and Hypertension. *(Postponed from February 25.)*
LONDON UNIVERSITY.—At Bedford College, Regent's Park, N.W., 5.15 p.m., special university lecture in philosophical studies by Professor R. Polin (Lille): Happiness.
ST. ANDREWS UNIVERSITY.—At Physiology Lecture Theatre, 5 p.m., Mr. J. F. Riley: Recipes for Research.
ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Mr. C. J. Dewhurst: Some Problems of Sex and Intersex.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., Dr. B. G. Parsons-Smith: neurological demonstration.

Wednesday, March 5

●CIBA FOUNDATION.—At Royal Society of Tropical Medicine and Hygiene, 5 p.m., 10th (Annual) Ciba Foundation Lecture by Professor Daniel Bovet (Rome): Experimental Basis of Neuroleptic and Tranquillizing Therapy.
INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. R. W. Riddell: Role of Yeasts in Skin Diseases.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. L. Livingstone: Open Lecture on Pros and Cons of Steroid Therapy for Asthma.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., Dr. J. Friedmann, Dr. D. A. Osborn, and Dr. S. Epstein: clinico-pathological conference.
INSTITUTE OF UROLOGY.—4.30 for 5 p.m., Dr. A. R. Harrison: Metabolic Bone Disease.
LONDON UNIVERSITY.—At Bedford College, Regent's Park, N.W., 5.15 p.m., special university lecture in philosophical studies by Professor R. Polin (Lille): Happiness.
MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., Dr. P. G. H. Gell: Paradox of Allergy.
OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Litchfield Lecture by Dr. J. F. Loutit: Successful Transplantation of Homologous and Heterologous Tissue in the Experimental Mouse.
PHYSICAL SOCIETY COLOUR GROUP.—At Lecture Theatre, Institute of Ophthalmology, 3.30 p.m., Commander Dean Farnsworth (U.S. Naval Research): How the World Looks to a Colour Blind.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—2 p.m., Dr. Cuthbert Dukes: Surgical Pathology of Rectal Cancer.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. J. C. Colligan: Rehabilitation, Training, and Employment of the Blind.

Thursday, March 6

LIVERPOOL MEDICAL INSTITUTION.—4.30 p.m., joint meeting with Manchester Medical Society. Dr. Ralston Paterson: Breast Cancer—Preliminary Report of Two Clinical Experiments; Mr. Ian Orr: Surgical Surprises in the Small Intestine.
MIDLAND THORACIC SOCIETY.—At Queen Elizabeth Hospital, Birmingham, Dr. E. G. L. Bywaters: Collagen Diseases as They Affect the Lungs.
ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Some Defects in Binocular Vision.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Sir Paul Mallinson: postgraduate demonstration in psychiatry.

Friday, March 7

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. E. J. Moynahan: clinical demonstration.
INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. H. Scadding: clinical demonstration.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—3.30 p.m., clinical discussion for general practitioners by Mr. Charles Heanley: Facial Reconstruction.
POSTGRADUATE MEDICAL SCHOOL OF LONDON.—(1) 10 a.m., Mr. H. S. Shucksmith: Surgery of Arteriosclerotic Arteries. (2) 4 p.m., Dr. R. E. Tunbridge: The So-called Collagen Diseases.
ROYAL MEDICAL SOCIETY, EDINBURGH.—8 p.m., President's Valedictory Address.
ROYAL MEDICO-CHIRURGICAL SOCIETY OF GLASGOW.—At Royal Faculty of Physicians and Surgeons of Glasgow, 8.30 p.m., Dr. J. E. Geddes and Dr. C. W. Clayson: Eradication of Tuberculous Disease.

APPOINTMENTS

LIVERPOOL REGIONAL HOSPITAL BOARD.—S. E. Keidan, M.B., Ch.B., M.R.C.P., D.C.H., Part-time Paediatrician in Department of Child Health, Alder Hey Children's Hospital; R. V. Tracy Forster, M.B., Ch.B., F.R.C.S., D.L.O., Part-time Consultant Ear, Nose, and Throat Surgeon, Southport Promenade Hospital; J. M. A. C. Stewart, M.B., Ch.B., D.P.M., Whole-time Assistant Psychiatrist, Rainhill Hospital.

MANCHESTER REGIONAL HOSPITAL BOARD.—R. S. Ferguson, M.D., D.P.M., Whole-time Consultant Psychiatrist and Deputy Medical Superintendent, Lancaster Moor Hospital; J. Firth, M.B., Ch.B., M.R.C.O.G., Consultant Obstetrician and Gynaecologist, Bolton and District Group of Hospitals; I. J. L. Goldberg, M.R.C.S., L.R.C.P., Whole-time Assistant Pathologist, Oldham and District Group of Hospitals; R. G. Williams, M.B., B.S., Whole-time Assistant Chest Physician, Wigan, Leigh, and Wrightington Hospital.

SHORT, IAN A., M.B., F.R.F.P.S., M.R.C.P., Part-time Consultant Physician at the Western Infirmary, Glasgow.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—C. P. Seager, M.B., B.Ch., D.P.M., Assistant Psychiatrist to Bristol Mental Hospitals Group; M. Y. Rai, M.B., B.S., F.R.C.S., F.R.C.S.Ed., Registrar to Orthopaedic Service, Exeter Clinical Area; J. Piggot, M.B., B.Ch., F.R.C.S.Ed., Research Assistant in Registrar Grade at Princess Elizabeth Orthopaedic Hospital, Exeter.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Fallon.—On February 17, 1958, at Glasgow Royal Maternity Hospital, to Valerie, M.P.S., and Ronald J. Fallon, M.D., a second daughter—Hilary Joy.

DEATHS

Barker.—On February 20, 1958, at the home of his son, 46, Brownlow Road, London, N., William Neish Barker, M.B., Ch.B., aged 81.
Beattie.—On February 15, 1958, Frederick Alexander Beattie, M.B., B.S., of Grosvenor Lodge, Seaford, Sussex, late of Lee, London, S.E., and Cleveleys, Lancs.
Beggs.—On February 13, 1958, William Beggs, M.D., F.R.C.S.Ed., late of St. George's, Oakengates, Salop.
Bickford.—On February 9, 1958, Nicholas Seymour Bickford, M.R.C.S., L.R.C.P., of Wimbledon.
Biggs.—On February 9, 1958, at Tiverton, Devon, Lesley Newton Hesketh Biggs, M.D.
Bokenham.—On February 15, 1958, Thomas Brandon Bokenham, M.R.C.S., L.R.C.P., of 22, Tennis Road, Hove, late of Worthing, Sussex.
Brown.—On February 8, 1958, James Leach Brown, M.R.C.S., L.R.C.P., of 160, Whitton Road, Hounslow.
Clay.—On February 5, 1958, the result of an accident, John Clay, M.B., B.S. (Jun.), of Letchworth, Herts.
Gethin Jones.—On February 8, 1958, at Glasgwm, Bettws-y-Coed, Caernarvonshire, Owen Gethin Jones, M.D.
Howat.—On February 9, 1958, at his home, 1-10, Northwood Hall, Hornsey Lane, Highgate, London, N., Robert King Howat, F.R.C.S., F.R.F.P.S.
Malim.—On February 6, 1958, at Rowley Road, St. Marychurch, Torquay, Jeffrey Wentworth Malim, M.B., B.Ch.
Milner.—On February 12, 1958, at 185, Millhouses Lane, Sheffield, Norton Milner, M.R.C.S., L.R.C.P.
Rothwell.—On February 10, 1958, in a nursing-home, Thomas George Rothwell, M.B., Ch.B.
Sebastian.—On February 12, 1958, Gerald Noel Boyd Sebastian, M.R.C.S., L.R.C.P., of Charlwood House, Charlwood, Surrey.
Shlosberg.—On February 9, 1958, Jacob Shlosberg, M.B., Ch.B., of "Winterfield," Bury New Road, Salford, 7.
Steel.—On February 3, 1958, at 48, Pettycur Road, Kinghorn, Fife, John Parker Steel, M.D., late of Liverpool, aged 66.
Stoker.—On February 10, 1958, at Watford, Herts, Frederick Octavius Stoker, L.R.C.P.&S., aged 91.
Thomas.—On February 9, 1958, at Penarth, Glam, George Nathaniel William Thomas, M.B., Ch.B., D.P.M.
Unsworth.—On February 10, 1958, in hospital, George Unsworth, M.B., Ch.B., of 21, Dean Road, Bolton.
Venniker.—On January 27, 1958, at Brighton, Sussex, John Charles Venniker, M.D., F.R.C.S.Ed., D.P.H., Lieutenant-Colonel, S.A.M.C., retired.
Wheaton.—On February 4, 1958, at Lambeth Hospital, London, S.E., Margaret Helena Wheaton (formerly Banks), M.R.C.S., L.R.C.P.
Winter.—On February 4, 1958, at his home, Gills Hill, Bourn, Cambs, Bedrich Winter, M.D.

Any Questions?

We publish below a selection of those questions and answers which seem of general interest. It is regretted that it is not possible to supply answers to all questions submitted.

Prophylactic Vaccines in Children Going Abroad

Q.—*What doses respectively of T.A.B., yellow fever, cholera, and typhus vaccine should be given, when indicated on epidemiological grounds, to infants and young children going abroad? Please indicate for each vaccine the earliest age at which it should be given.*

A.—Vaccination against yellow fever may be legally required of infants and children of all ages as a condition of entry into an endemic region. It may therefore have to be carried out at birth, but in view of the greater risk of encephalitis occurring as one of its complications in early life it is desirable, whenever possible, to postpone vaccination till the age of 9 months. The standard dose must be used for persons of all ages. Yellow fever vaccination should always precede primary smallpox vaccination, and it is desirable that it should precede non-primary smallpox vaccination by an interval of at least four days.

Customary practice is not to vaccinate against smallpox before the age of 3 months and against enteric fever, cholera, and typhus before the age of 1 year. For children aged 1–14 years half the adult dosage of these vaccines is given. The vaccine customarily in use for enteric fever contains 1,000,000,000 *Salmonella typhi* and 500,000,000 *S. paratyphi* A and B in each ml. Previously unvaccinated children would normally receive an initial injection of 0.25 ml., followed after an interval of one week by an injection of 0.5 ml. The customarily used cholera vaccine contains 8,000,000,000 *Vibrio cholerae* per ml., and of this unvaccinated children should receive 0.25 ml. followed in a week by a second injection of 0.5 ml. Vaccines for use against scrub typhus are at present prepared from local strains only in certain laboratories in the tropics, but one of value against murine and louseborne typhus is prepared by Connaught Medical Laboratories, Toronto, Canada, and of this the dose for children would be two injections each of 0.5 ml. separated by an interval of one week.

Further details concerning vaccination and the sequence and spacing of vaccinations may be found in the *Supplement* to *Paediatrics for the Practitioner*,[1] and in the *Transactions of the Association of Industrial Medical Officers*.[2]

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[1] Gaisford, W., and Lightwood, R. (editors), *Paediatrics for the Practitioner*, 1956, supplement. Butterworth, London.
[2] Woodruff, A. W., *Trans. Ass. industr. med. Offrs*, 1952, **2**, 158.

Immunization and Anaphylactic Shock

Q.—*What is the dosage and technique of administration of adrenaline in a case of anaphylactic shock in (1) an infant of 3–9 months after being immunized for the first time; (2) an older child of about 5 years who has received a booster immunization?*

A.—Anaphylactic shock may occur after some but not all prophylactic immunizations. In the case of prophylactic (passive) immunization against either tetanus or diphtheria with antitoxin the risks of anaphylaxis are real, and the procedure to be adopted, (1) before giving the injection, and (2) for the treatment of anaphylactic shock should it develop, has been described by Laurent and Parish[1] and Parish *et al.*[2] In the case of human gamma globulin for prophylaxis against measles, etc., anaphylactic shock does not occur.

In the case of the diphtheria prophylactics, purified F.T., A.P.T., and P.T.A.P., and in the case of tetanus toxoid, the risks of anaphylactic shock are negligible. However, after T.A.F.—which contains a small amount of horse serum—anaphylactic shock may occur, especially in subjects of the asthma-eczema group; these should not be immunized with T.A.F. Anaphylactic shock very rarely may follow T.A.B. vaccine, pertussis vaccine, and streptococcal toxin. It has not been described after poliomyelitis vaccine (Salk type), but may occur after influenza virus vaccine and yellow-fever vaccine if the subject is allergic to egg. The pathogenesis of the extremely rare "encephalopathy" which has followed certain immunizing antigens, especially pertussis vaccine, is obscure; the symptoms are not those of anaphylactic shock and adrenaline is unlikely to be useful.

In the presence of a severe case of anaphylactic shock the initial dose of solution of adrenaline, 1 in 1,000, should be 0.5 ml. for an infant or for a child up to 12 years of age. The injection should be given immediately *deeply into a muscle*, either the vastus externus in the middle third of the thigh or into the triceps. Subsequent doses, if necessary, should be half the initial dose. The dose and the procedure are the same whether the reaction follows a first injection or a booster injection. At all immunization clinics sterile 1 ml. syringes, intramuscular needles, and ampoules of 0.5 ml. of adrenaline, 1 in 1,000, should always be handy for an emergency. The prevention of anaphylactic shock is just as important as its immediate treatment. Both aspects of the subject are fully dealt with in the articles mentioned above.

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[1] Laurent, L. J. M., and Parish, H. J., *Brit. med. J.*, 1952, **1**, 1294.
[2] Parish, H. J., Laurent, L. J. M., and Moynihan, N. H., ibid., 1957, **1**, 639.

Surgery in Emphysema

Q.—*Has surgery any place in the management of pulmonary emphysema?*

A.—Two types of operation have been tried in pulmonary emphysema. The first consists of operations upon the nerve plexuses associated with the lungs in patients with generalized emphysema. The hypothesis is that interruption of the autonomic nerve supply may relax bronchial spasm, and that this may be helpful either in arresting the progress of the emphysema or simply in causing symptomatic relief. On the whole, these operations have met with very little success, and the theoretical basis for them cannot be regarded as established. The second type of operation is applicable only to the very small minority of patients in whom localized bullous emphysema is contributing largely to the dyspnoea. In such cases there will usually be easily detected physical and radiological signs of the localized abnormality. The breath sounds over the affected part of the lung will be weak as compared with the less affected parts, and radiologically the affected part will be notably more transradiant than the rest of the lung, with very few vascular markings, and may appear as an actual thin-walled cyst. On fluoroscopy little or no change will be seen in the size of the abnormally transradiant area with respiration, air being trapped in it during expiration with displacement of the mediastinum towards the normal side. In such cases the affected part of the lung is a very much smaller fraction of the lung than its size in its distended bullous state would suggest. When it is distended to such an extent that it interferes with ventilation of the less affected parts of the lungs its surgical removal may diminish the dyspnoea. The benefit to be derived from such an operation can be judged nearly as well from a clinical and radiological estimate of the mechanics of the situation as from elaborate physiological tests. On the whole, there are very few patients with emphysema for whom surgery has anything to offer at present.

Treatment of Intermittent Claudication

Q.—*What is the modern treatment of intermittent claudication, and what results may be expected from it?*

A.—Intermittent claudication is a symptom produced by a variety of causes including arterial diseases and anaemia. In the majority of patients the cause is thrombosis of a major

artery owing to atherosclerosis; here only the treatment of patients suffering from intermittent claudication due to this disease will be discussed.

Atherosclerosis is a general disease, and it is important to realize that intermittent claudication is only a local manifestation of a general abnormality. Treatment may be medical or surgical. Medical measures include correction of anaemia, reduction of weight, stopping tobacco-smoking, and the use of vasodilator drugs. Surgical measures include sympathectomy and arterial reconstruction operations.

In many patients it is a mistake to treat intermittent claudication too actively. For example, a successful arterial reconstruction operation may cure this symptom, only for the patient to be stopped by the worse pain of angina pectoris after he has walked a little further than he did before the operation. However, for those patients with severe symptoms and particularly those who cannot work, active measures are desirable. A bypass type of arterial reconstruction operation is the best method of surgical treatment, and, if successful, results in complete relief.

Hyperpyrexia and Survival

Q.—*What are the highest temperatures in children compatible with survival?*

A.—Children are apt to run higher temperatures than adults, but there is no good reason to believe that extreme hyperpyrexia is tolerated better or worse in children than in adults. In adults, Rogers[1] studied the mortality of heat stroke and found it, in two series of cases, to be 8.3% when the body temperature was less than 107° F. (41.7° C.), 29.2% when the temperature was between 107° and 109° F. (41.7–42.8° C.), and 69.2% when the body temperature exceeded 109° F. (42.8° C.). Body temperatures of 112° F. (44.4° C.) with survival have been quoted in the literature.[2] The same degree of fever is recorded in children.[3] A case of hyperpyrexia following a Turkish bath in an adult was reported in last week's *Journal* (p. 443).

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1. Rogers, L., quoted in *Tropical Medicine*, by Rogers, L., Megaw, J. D. W., and McRobert, G. R., 1952. Churchill, London.
2. Marsh, F., *Lancet*, 1930, **2**, 904.
3. Héritier, P., *Arch. de Méd. d. enf.*, 1930, **33**, 29.

Amoebic Cysts in Drinking-water

Q.—*Is chlorination of drinking-water an adequate safeguard against amoebic cysts?*

A.—Chlorination of drinking-water is not an adequate safeguard against amoebic cysts, and no satisfactory chemical method of eradicating them from drinking-water has yet been devised and proved. Boiling the water remains the only completely satisfactory procedure, but the use of well-maintained Berkefeld filters will also eliminate cysts. It is essential that the filters should be thoroughly cleaned every two to three days, for otherwise there is grave risk of bacterial and other infection of the water which has passed through them.

Antiseptic Powder for Minor Wounds

Q.—*Sensitization to penicillin may follow the use of penicillin and sulphathiazole powder in treating minor wounds. What other antiseptic powder may be used?*

A.—If a powder is insisted on, and assuming that possible sensitization to sulphathiazole is not regarded in the same light as sensitization to penicillin, an effective substitute would be a powder containing 1 part of proflavine hemisulphate in 99 parts of sulphathiazole. This was extensively used before penicillin became available, and its efficacy in preventing sepsis has been proved.

There are many alternatives for the antiseptic treatment of minor injuries apart from the use of a powder. It may often be considered enough to swab out the lesion with a solution of a quaternary ammonium compound such as 1% cetrimide: this has an excellent cleansing action as well as some antiseptic effect. A more powerful antiseptic suitable for this kind of use is hibitane, which may be applied as a 2.5% aqueous solution, as a 1% cream, or in a lower concentration in a solution combined with cetrimide. Either a powder or a cream has a much more lasting effect than swabbing or irrigating with a solution, and may be preferred when there is any actual reason for suspecting contamination by pyogenic bacteria.

Laying Out the Dead

Q.—*Why do nurses occlude all orifices with cotton-wool when laying out the dead?*

A.—After death a body is carefully washed and wrapped in a clean covering. The orifices are stopped up to avoid the escape of discharges, which otherwise might befoul the clean covering and in some cases might even spread infection. This simple act is therefore a useful sanitary precaution.

Thyroid Treatment for Otosclerosis

Q.—*Is thyroid extract or oral iodine of value in the treatment of otosclerosis?*

A.—Some years ago there was a fashion for injecting thyroxine into the tympanum in cases of deafness due to otosclerosis, the idea being to cause dilatation of the blood vessels in the bony capsule of the labyrinth. The results of this medication were not sufficiently encouraging to keep it from falling into disuse. Thyroid gland extract by mouth and iodine by mouth have been used for otosclerosis, but again the results have been in some doubt and these drugs are not now regularly used.

Otosclerosis is a disease of bone, and the otosclerotic patch of bone appears on the bony capsule of the labyrinth. The favourite site is the small fissure just in front of the oval window, which is often filled with cartilage. It is thought that as the bony labyrinth is fully developed at birth the otosclerotic bone is an attempt on the part of nature to turn any little patches of cartilage into bone, and this is brought about by bone-growth-promoting substances circulating in the blood. During adolescence or during the last two months of pregnancy are favourite times for otosclerosis to begin or get worse, and it is at just these times that cartilage is being turned into bone. It is possible that in some cases iodine or thyroid might interfere with this growth of bone mechanism, in which case a regression of the deafness can be explained.

NOTES AND COMMENTS

Corrections.—In the leading article on acute otitis media (*Journal*, February 8, p. 328) it was said that among J. A. H. Lee's cases of candidates for National Service rejected because of ear discharge a "high proportion" had cholesteatosis. This was incorrect, and in fact he found the condition to be rare.

The peak-flow meter referred to by Dr. J. L. Livingstone (*Journal*, February 22, p. 454) should have been described as designed by Dr. B. M. Wright.

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